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(54) Title: COMPOUNDS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF *B. MICROTI* INFECTION

(57) Abstract

Compounds and methods for the diagnosis and treatment of *B. microti* infection are disclosed. The compounds provided include polypeptides that contain at least one antigenic portion of a *B. microti* antigen and DNA sequences encoding such polypeptides. Antigenic epitopes of such antigens are also provided, together with pharmaceutical compositions and vaccines comprising such polypeptides, DNA sequences or antigenic epitopes. Diagnostic kits containing such polypeptides, DNA sequences or antigenic epitopes and a suitable detection reagent may be used for the detection of *B. microti* infection in patients and biological samples. Antibodies directed against such polypeptides and antigenic epitopes are also provided.

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COMPOUNDS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF *B. MICROTI* INFECTION

TECHNICAL FIELD

The present invention relates generally to the detection of *Babesia microti* infection. In particular, the invention is related to polypeptides comprising a *B. microti* antigen, to antigenic epitopes of such an antigen and the use of such polypeptides and antigenic epitopes for the serodiagnosis and treatment of *B. microti* infection.

BACKGROUND OF THE INVENTION

Babesiosis is a malaria-like illness caused by the rodent parasite *Babesia microti* (*B. microti*) which is generally transmitted to humans by the same tick that is responsible for the transmission of Lyme disease and ehrlichiosis, thereby leading to the possibility of co-infection with babesiosis, Lyme disease and ehrlichiosis from a single tick bite. While the number of reported cases of *B. microti* infection in the United States is increasing rapidly, infection with *B. microti*, including co-infection with Lyme disease, often remains undetected for extended periods of time. Babesiosis is potentially fatal, particularly in the elderly and in patients with suppressed immune systems. Patients infected with both Lyme disease and babesiosis have more severe symptoms and prolonged illness compared to those with either infection alone.

The preferred treatments for Lyme disease, ehrlichiosis and babesiosis are different, with penicillins, such as doxycycline and amoxicillin, being most effective in treating Lyme disease, tetracycline being preferred for the treatment of ehrlichiosis, and anti-malarial drugs, such as quinine and clindamycin, being most effective in the treatment of babesiosis. Accurate and early diagnosis of *B. microti* infection is thus critical but methods currently employed for diagnosis are problematic.

All three tick-borne illnesses share the same flu-like symptoms of muscle aches, fever, headaches and fatigue, thus making clinical diagnosis difficult. Microscopic analysis of blood samples may provide false-negative results when patients

are first seen in the clinic. Indirect fluorescent antibody staining methods for total immunoglobulins to *B. microti* may be used to diagnose babesiosis infection, but such methods are time-consuming and expensive. There thus remains a need in the art for improved methods for the detection of *B. microti* infection.

SUMMARY OF THE INVENTION

The present invention provides compositions and methods for the diagnosis and treatment of *B. microti* infection. In one aspect, polypeptides are provided comprising an immunogenic portion of a *B. microti* antigen, or a variant of such an antigen that differs only in conservative substitutions and/or modifications. In one embodiment, the antigen comprises an amino acid sequence encoded by a DNA sequence selected from the group consisting of (a) sequences recited in SEQ ID NO: 1-17, 37, 40, 42, 45, 50 and 51; (b) the complements of said sequences; and (c) sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

In another aspect, the present invention provides an antigenic epitope of a *B. microti* antigen comprising the amino acid sequence -X_1-X_2-X_3-X_4-X_5-Ser- (SEQ ID NO: 35), wherein X_1 is Glu or Gly, X_2 is Ala or Thr, X_3 is Gly or Val, X_4 is Trp or Gly and X_5 is Pro or Ser. In one embodiment of this aspect, X_1 is Glu, X_2 is Ala and X_3 is Gly. In a second embodiment X_1 is Gly, X_2 is Thr and X_5 is Pro. The present invention further provides polypeptides comprising at least two of the above antigenic epitopes, the epitopes being contiguous.

In yet another aspect, the present invention provides an antigenic epitope of a *B. microti* antigen comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 36 and 39, together with polypeptides comprising at least two such antigenic epitopes, the epitopes being contiguous.

In a related aspect, polynucleotides encoding the above polypeptides, recombinant expression vectors comprising these polynucleotides and host cells transformed or transfected with such expression vectors are also provided.

In another aspect, the present invention provides fusion proteins comprising either a first and a second inventive polypeptide, a first and a second inventive antigenic epitope, or, alternatively, an inventive polypeptide and an inventive

antigenic epitope. In specific embodiments, fusion proteins comprising an amino acid sequence of SEQ ID NO: 85 or 87 are provided.

In further aspects of the subject invention, methods and diagnostic kits are provided for detecting *B. microti* infection in a patient. In one embodiment, the method comprises: (a) contacting a biological sample with at least one polypeptide comprising an immunogenic portion of a *B. microti* antigen; and (b) detecting in the sample the presence of antibodies that bind to the polypeptide, thereby detecting *B. microti* infection in the biological sample. In other embodiments, the methods comprise: (a) contacting a biological sample with at least one of the above polypeptides or antigenic epitopes; and (b) detecting in the sample the presence of antibodies that bind to the polypeptide or antigenic epitope. Suitable biological samples include whole blood, sputum, serum, plasma, saliva, cerebrospinal fluid and urine. The diagnostic kits comprise one or more of the above polypeptides or antigenic epitopes in combination with a detection reagent.

The present invention also provides methods for detecting *B. microti* infection comprising: (a) obtaining a biological sample from a patient; (b) contacting the sample with at least two oligonucleotide primers in a polymerase chain reaction, at least one of the oligonucleotide primers being specific for a DNA sequence encoding the above polypeptides; and (c) detecting in the sample a DNA sequence that amplifies in the presence of the first and second oligonucleotide primers. In one embodiment, the oligonucleotide primer comprises at least about 10 contiguous nucleotides of a DNA sequence encoding the above polypeptides.

In a further aspect, the present invention provides a method for detecting *B. microti* infection in a patient comprising: (a) obtaining a biological sample from the patient; (b) contacting the sample with an oligonucleotide probe specific for a DNA sequence encoding the above polypeptides; and (c) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe. In one embodiment of this aspect, the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a DNA sequence encoding the above polypeptides.

In yet another aspect, the present invention provides antibodies, both polyclonal and monoclonal, that bind to the polypeptides described above, as well as methods for their use in the detection of *B. microti* infection.

Within other aspects, the present invention provides pharmaceutical compositions that comprise one or more of the above polypeptides or antigenic epitopes, or a polynucleotide encoding such polypeptides, and a physiologically acceptable carrier. The invention also provides vaccines comprising one or more of the inventive polypeptides or antigenic epitopes and a non-specific immune response enhancer, together with vaccines comprising one or more polynucleotides encoding such polypeptides and a non-specific immune response enhancer.

In yet another aspect, methods are provided for inducing protective immunity in a patient, comprising administering to a patient an effective amount of one or more of the above pharmaceutical compositions or vaccines.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows the genomic sequence of the *B. microti* antigen BMNI-3 (SEQ ID NO: 3) including a translation of the putative open reading frame (SEQ ID NO: 49). An internal six amino acid repeat sequence (SEQ ID NO: 35) is indicated by vertical lines within the open reading frame.

Fig. 2a shows the reactivity of the *B. microti* antigens BMNI-3 and BMNI-6, and the peptides BABS-1 and BABS-4 with sera from *B. microti*-infected individuals and from normal donors as determined by ELISA. Fig. 2b shows the reactivity of the *B. microti* antigens BMNI-4 and BMNI-15 with sera from *B. microti*-infected individuals and from normal donors as determined by ELISA.

Fig. 3 shows the reactivity of the *B. microti* antigens MN-10 and BMNI-20 with sera from *B. microti*-infected patients and from normal donors as determined by ELISA.

Fig. 4 shows the results of Western blot analysis of representative *B. microti* antigens of the present invention.

Fig. 5 shows the reactivity of purified recombinant *B. microti* antigen BMNI-3 with sera from *B. microti*-infected patients, Lyme disease-infected patients, ehrlichiosis-infected patients and normal donors as determined by Western blot analysis.

Fig. 6 shows an alignment of the repeat region of different homologues of the *B. microti* antigen BMNI-6, illustrating the geographic variation in the number and location of the repeats.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the diagnosis and treatment of *B. microti* infection. In one aspect, the compositions of the subject invention include polypeptides that comprise at least one immunogenic portion of a *B. microti* antigen, or a variant of such an antigen that differs only in conservative substitutions and/or modifications.

As used herein, the term "polypeptide" encompasses amino acid chains of any length, including full length proteins (*i.e.*, antigens), wherein the amino acid residues are linked by covalent peptide bonds. Thus, a polypeptide comprising an immunogenic portion of one of the above antigens may consist entirely of the immunogenic portion, or may contain additional sequences. The additional sequences may be derived from the native *B. microti* antigen or may be heterologous, and such sequences may (but need not) be immunogenic.

An "immunogenic portion" of an antigen is a portion that is capable of reacting with sera obtained from a *B. microti*-infected individual (*i.e.*, generates an absorbance reading with sera from infected individuals that is at least three standard deviations above the absorbance obtained with sera from uninfected individuals, in a representative ELISA assay described herein). Polypeptides comprising at least an immunogenic portion of one or more *B. microti* antigens as described herein may generally be used, alone or in combination, to detect *B. microti* in a patient.

Polynucleotides encoding the inventive polypeptides are also provided. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides. Such variants include, but are not limited to, naturally occurring allelic variants of the inventive sequences.

A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described below) to the identified polypeptides.

As used herein, a "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. In general, the following groups of amino acids represent conservative changes: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his.

Variants may also, or alternatively, contain other modifications, including the deletion or addition of amino acids that have minimal influence on the antigenic properties, secondary structure and hydropathic nature of the polypeptide. For

example, a polypeptide may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

A polynucleotide "variant" is a sequence that differs from the recited polynucleotide sequence in having one or more nucleotide deletions, substitutions or additions. Such modifications may be readily introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis as taught, for example, by Adelman et al. (*DNA*, *2*:183, 1983). Polynucleotide variants may be naturally occurring allelic variants, or non-naturally occurring variants. Variant polynucleotide sequences preferably exhibit at least about 70%, more preferably at least about 80% and most preferably at least about 90% identity (determined as described below) to the recited sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Resarch Foundaiton, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990)

Unified Approach to Alignment and Phylogenes pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS 5*:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS 4*:11-17; Robinson, E.D. (1971) *Comb. Theor 11*:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol. 4*:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad., Sci. USA 80*:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (i.e. gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (i.e. the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

In specific embodiments, the subject invention discloses polypeptides comprising at least an immunogenic portion of a *B. microti* antigen (or a variant of such an antigen), that comprises one or more of the amino acid sequences encoded by (a) a DNA sequence selected from the group consisting of SEQ ID NO: 1-17, 37, 40, 42, 45 50, 51 and 56-67, (b) the complements of such DNA sequences or (c) DNA sequences substantially homologous to a sequence of (a) or (b).

The *B. microti* antigens provided by the present invention include variants that are encoded by polynucleotides which are substantially homologous to one or more of the polynucleotides specifically recited herein. "Substantial homology," as used herein, refers to polynucleotides that are capable of hybridizing under moderately

stringent conditions. Suitable moderately stringent conditions include prewashing in a solution of 5X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing polynucleotides are also within the scope of this invention, as are polynucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing polynucleotide.

In general, *B. microti* antigens, and polynucleotides encoding such antigens, may be prepared using any of a variety of procedures. For example, polynucleotides encoding *B. microti* antigens may be isolated from a *B. microti* genomic or cDNA expression library by screening with sera from *B. microti*-infected individuals as described below in Example 1, and sequenced using techniques well known to those of skill in the art. Polynucleotides encoding *B. microti* antigens may also be isolated by screening an appropriate *B. microti* expression library with anti-sera (*e.g.*, rabbit) raised specifically against *B. microti* antigens.

Antigens may be induced from such clones and evaluated for a desired property, such as the ability to react with sera obtained from a *B. microti*-infected individual as described herein. Alternatively, antigens may be produced recombinantly, as described below, by inserting a polynucleotide that encodes the antigen into an expression vector and expressing the antigen in an appropriate host. Antigens may be partially sequenced using, for example, traditional Edman chemistry. *See* Edman and Berg, *Eur. J. Biochem. 80*:116-132, 1967.

Polynucleotides encoding antigens may also be obtained by screening an appropriate *B. microti* cDNA or genomic DNA library for polynucleotides that hybridize to degenerate oligonucleotides derived from partial amino acid sequences of isolated antigens. Degenerate oligonucleotides for use in such a screen may be designed and synthesized, and the screen may be performed, as described (for example) in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (and references cited therein). Polymerase chain reaction (PCR) may also be employed, using the above oligonucleotides in methods

well known in the art, to isolate a nucleic acid probe from a cDNA or genomic library. The library screen may then be performed using the isolated probe.

Synthetic polypeptides having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc. 85*:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division, Foster City, CA, and may be operated according to the manufacturer's instructions.

Immunogenic portions of *B. microti* antigens may be prepared and identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3d ed., Raven Press, 1993, pp. 243-247 and references cited therein. Such techniques include screening polypeptide portions of the native antigen for immunogenic properties. The representative ELISAs described herein may generally be employed in these screens. An immunogenic portion of a polypeptide is a portion that, within such representative assays, generates a signal in such assays that is substantially similar to that generated by the full length antigen. In other words, an immunogenic portion of a *B. microti* antigen generates at least about 20%, and preferably about 100%, of the signal induced by the full length antigen in a model ELISA as described herein.

Portions and other variants of *B. microti* antigens may be generated by synthetic or recombinant means. Variants of a native antigen may generally be prepared using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis. Sections of the DNA sequence may also be removed using standard techniques to permit preparation of truncated polypeptides.

Recombinant polypeptides containing portions and/or variants of a native antigen may be readily prepared from a polynucleotide encoding the polypeptide using a variety of techniques well known to those of ordinary skill in the art. For example, supernatants from suitable host/vector systems which secrete recombinant

protein into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant protein.

Any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides as described herein. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line, such as COS or CHO. The polynucleotides expressed in this manner may encode naturally occurring antigens, portions of naturally occurring antigens, or other variants thereof.

In another aspect, the present invention provides epitope repeat sequences, or antigenic epitopes, of a *B. microti* antigen, together with polypeptides comprising at least two such contiguous antigenic epitopes. As used herein an "epitope" is a portion of an antigen that reacts with sera from *B. microti*-infected individuals (i.e. an epitope is specifically bound by one or more antibodies present in such sera). As discussed above, epitopes of the antigens described in the present application may be generally identified using techniques well known to those of skill in the art.

In one embodiment, antigenic epitopes of the present invention comprise the amino acid sequence $-X_1-X_2-X_3-X_4-X_5-$Ser- (SEQ ID NO: 35), wherein X_1 is Glu or Gly, X_2 is Ala or Thr, X_3 is Gly or Val, X_4 is Trp or Gly, and X_5 is Pro or Ser. In another embodiment, the antigenic epitopes of the present invention comprise an amino acid sequence selected from the group consisting of SEQ ID NO: 36 and 39. As discussed in more detail below, antigenic epitopes provided herein may be employed in the diagnosis and treatment of *B. microti* infection, either alone or in combination with other *B. microti* antigens or antigenic epitopes. Antigenic epitopes and polypeptides

comprising such epitopes may be prepared by synthetic means, as described generally above and in detail in Example 2.

In general, regardless of the method of preparation, the polypeptides, polynucleotides and antigenic epitopes disclosed herein are prepared in an isolated, substantially pure, form. Preferably, the polypeptides and antigenic epitopes are at least about 80% pure, more preferably at least about 90% pure and most preferably at least about 99% pure.

In a further aspect, the present invention provides fusion proteins comprising either a first and a second inventive polypeptide, a first and a second inventive antigenic epitope or an inventive polypeptide and an antigenic epitope of the present invention, together with variants of such fusion proteins. The fusion proteins of the present invention may also include a linker peptide between the polypeptides or antigenic epitopes.

A polynucleotide encoding a fusion protein of the present invention is constructed using known recombinant DNA techniques to assemble separate polynucleotides encoding, for example, the first and second polypeptides into an appropriate expression vector. The 3' end of a polynucleotide encoding the first polypeptide is ligated, with or without a peptide linker, to the 5' end of a polynucleotide encoding the second polypeptide so that the reading frames of the sequences are in phase to permit mRNA translation of the two polynucleotides into a single fusion protein that retains the biological activity of both the first and the second polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptides by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the

linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene 40*:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA 83*:8258-8562, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may be from 1 to about 50 amino acids in length. Peptide linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric hindrance.

In another aspect, the present invention provides methods for using polypeptides comprising an immunogenic portion of a *B. microti* antigen and/or the antigenic epitopes described above to diagnose babesiosis. In this aspect, methods are provided for detecting *B. microti* infection in a biological sample, using one or more of the above polypeptides and antigenic epitopes, alone or in combination. For clarity, the term "polypeptide" will be used when describing specific embodiments of the inventive diagnostic methods. However, it will be clear to one of skill in the art that the antigenic epitopes of the present invention may also be employed in such methods.

As used herein, a "biological sample" is any antibody-containing sample obtained from a patient. Preferably, the sample is whole blood, sputum, serum, plasma, saliva, cerebrospinal fluid or urine. More preferably, the sample is a blood, serum or plasma sample obtained from a patient. The polypeptides are used in an assay, as described below, to determine the presence or absence of antibodies to the polypeptide(s) in the sample, relative to a predetermined cut-off value. The presence of such antibodies indicates previous sensitization to *B. microti* antigens which may be indicative of babesiosis.

In embodiments in which more than one polypeptide is employed, the polypeptides used are preferably complementary (*i.e.*, one component polypeptide will tend to detect infection in samples where the infection would not be detected by another component polypeptide). Complementary polypeptides may generally be identified by using each polypeptide individually to evaluate serum samples obtained from a series of patients known to be infected with *B. microti*. After determining which samples test positive (as described below) with each polypeptide, combinations of two or more

polypeptides may be formulated that are capable of detecting infection in most, or all, of the samples tested.

A variety of assay formats are known to those of ordinary skill in the art for using one or more polypeptides to detect antibodies in a sample. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988, which is incorporated herein by reference. In a preferred embodiment, the assay involves the use of polypeptide immobilized on a solid support to bind to and remove the antibody from the sample. The bound antibody may then be detected using a detection reagent that contains a reporter group. Suitable detection reagents include antibodies that bind to the antibody/polypeptide complex and free polypeptide labeled with a reporter group (*e.g.*, in a semi-competitive assay). Alternatively, a competitive assay may be utilized, in which an antibody that binds to the polypeptide is labeled with a reporter group and allowed to bind to the immobilized antigen after incubation of the antigen with the sample. The extent to which components of the sample inhibit the binding of the labeled antibody to the polypeptide is indicative of the reactivity of the sample with the immobilized polypeptide.

The solid support may be any solid material known to those of ordinary skill in the art to which the antigen may be attached. For example, the solid support may be a test well in a microtiter plate, or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681.

The polypeptides may be bound to the solid support using a variety of techniques known to those of ordinary skill in the art. In the context of the present invention, the term "bound" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent). Binding by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the polypeptide, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies

with temperature, but is typically between about 1 hour and 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of polypeptide ranging from about 10 ng to about 1 μg, and preferably about 100 ng, is sufficient to bind an adequate amount of antigen.

Covalent attachment of polypeptide to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the polypeptide. For example, the polypeptide may be bound to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the polypeptide (*see*, *e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is an enzyme linked immunosorbent assay (ELISA). This assay may be performed by first contacting a polypeptide antigen that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that antibodies to the polypeptide within the sample are allowed to bind to the immobilized polypeptide. Unbound sample is then removed from the immobilized polypeptide and a detection reagent capable of binding to the immobilized antibody-polypeptide complex is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific detection reagent.

More specifically, once the polypeptide is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin (BSA) or Tween 20™ (Sigma Chemical Co., St. Louis, MO) may be employed. The immobilized polypeptide is then incubated with the sample, and antibody is allowed to bind to the antigen. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is that period of time that is sufficient to detect the presence of antibody within a *B. microti*-infected sample. Preferably, the contact time is sufficient to achieve a level of binding that is at least 95% of that achieved at equilibrium between bound and unbound antibody. Those of ordinary skill

in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. Detection reagent may then be added to the solid support. An appropriate detection reagent is any compound that binds to the immobilized antibody-polypeptide complex and that can be detected by any of a variety of means known to those in the art. Preferably, the detection reagent contains a binding agent (such as, for example, Protein A, Protein G, immunoglobulin, lectin or free antigen) conjugated to a reporter group. Preferred reporter groups include enzymes (such as horseradish peroxidase), substrates, cofactors, inhibitors, dyes, radionuclides, luminescent groups, fluorescent groups and biotin. The conjugation of binding agent to reporter group may be achieved using standard methods known to those of ordinary skill in the art. Common binding agents may also be purchased conjugated to a variety of reporter groups from many commercial sources (*e.g.*, Zymed Laboratories, San Francisco, CA, and Pierce, Rockford, IL).

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound antibody. An appropriate amount of time may generally be determined from the manufacturer's instructions or by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of anti-*B. microti* antibodies in the sample, the signal detected from the reporter group that remains bound to the solid

support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment. the cut-off value is the average mean signal obtained when the immobilized antigen is incubated with samples from an uninfected patient. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for babesiosis. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, pp. 106-107. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for babesiosis.

In a related embodiment, the assay is performed in a rapid flow-through or strip test format, wherein the antigen is immobilized on a membrane, such as nitrocellulose. In the flow-through test, antibodies within the sample bind to the immobilized polypeptide as the sample passes through the membrane. A detection reagent (*e.g.*, protein A-colloidal gold) then binds to the antibody-polypeptide complex as the solution containing the detection reagent flows through the membrane. The detection of bound detection reagent may then be performed as described above. In the strip test format, one end of the membrane to which polypeptide is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing detection reagent and to the area of immobilized polypeptide. Concentration of detection reagent at the polypeptide indicates the presence of anti-*B. microti* antibodies in the sample. Typically, the concentration of detection reagent at that site generates a pattern, such as a line, that can be read visually. The absence of

such a pattern indicates a negative result. In general, the amount of polypeptide immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of antibodies that would be sufficient to generate a positive signal in an ELISA, as discussed above. Preferably, the amount of polypeptide immobilized on the membrane ranges from about 25 ng to about 1 µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount (*e.g.*, one drop) of patient serum or blood.

Of course, numerous other assay protocols exist that are suitable for use with the polypeptides and antigenic epitopes of the present invention. The above descriptions are intended to be exemplary only.

In yet another aspect, the present invention provides antibodies to the polypeptides and antigenic epitopes of the present invention. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988. In one such technique, an immunogen comprising the antigenic polypeptide or epitope is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep and goats). The polypeptides and antigenic epitopes of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide or antigenic epitope may then be purified from such antisera by, for example, affinity chromatography using the polypeptide or antigenic epitope coupled to a suitable solid support.

Monoclonal antibodies specific for the antigenic polypeptide or epitope of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol. 6*:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide or antigenic epitope of

interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and tested for binding activity against the polypeptide or antigenic epitope. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides or antigenic epitopes of this invention may be used in the purification process in, for example, an affinity chromatography step.

Antibodies may be used in diagnostic tests to detect the presence of *B. microti* antigens using assays similar to those detailed above and other techniques well known to those of skill in the art, thereby providing a method for detecting *B. microti* infection in a patient.

Diagnostic reagents of the present invention may also comprise oligonucleotides encoding one or more of the above polypeptides, or one or more portions thereof. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify *B. microti*-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (i.e. hybridizes to) a polynucleotide encoding a polypeptide of the present invention. The presence of the amplified cDNA is then detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that

specifically hybridize to a polynucleotide encoding a polypeptide of the present invention may be used in a hybridization assay to detect the presence of an inventive polypeptide in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding an inventive polypeptide that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a polynucleotide of the present invention. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, *51*:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an uninfected individual. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-infected sample is typically considered positive.

Primers or probes may thus be used to detect *B. microti*-specific sequences in biological samples, preferably sputum, blood, serum, saliva, cerebrospinal fluid or urine. Oligonucleotide primers and probes may be used alone or in combination with each other.

In another aspect, the present invention provides methods for using one or more of the above polypeptides, antigenic epitopes or fusion proteins (or polynucleotides encoding such polypeptides) to induce protective immunity against *B. microti* infection in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may be afflicted with a disease, or may be free of detectable disease and/or infection. In other words, protective immunity may be induced to prevent or treat babesiosis.

In this aspect, the polypeptide, antigenic epitope, fusion protein or polynucleotide is generally present within a pharmaceutical composition or a vaccine. Pharmaceutical compositions may comprise one or more polypeptides, each of which may contain one or more of the above sequences (or variants thereof), and a physiologically acceptable carrier. Vaccines may comprise one or more of the above polypeptides and a non-specific immune response enhancer, such as an adjuvant or a liposome (into which the polypeptide is incorporated). Such pharmaceutical compositions and vaccines may also contain other *B. microti* antigens, either incorporated into a combination polypeptide or present within a separate polypeptide.

Alternatively, a vaccine may contain a polynucleotide encoding one or more polypeptides, antigenic epitopes or fusion proteins as described above, such that the polypeptide is generated *in situ*. In such vaccines, the polynucleotide may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacterial and viral expression systems. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface. In a preferred embodiment, the polynucleotide may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Techniques for incorporating polynucleotides into such expression systems are well known to those of ordinary skill in the art. The polynucleotide may also be "naked," as described, for example, in Ulmer et al., *Science 259*:1745-1749,

1993 and reviewed by Cohen, *Science 259*:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

In a related aspect, a DNA vaccine as described above may be administered simultaneously with or sequentially to either a polypeptide of the present invention or a known *B. microti* antigen. For example, administration of a polynucleotide encoding a polypeptide of the present invention, either "naked" or in a delivery system as described above, may be followed by administration of an antigen in order to enhance the protective immune effect of the vaccine.

Routes and frequency of administration, as well as dosage, will vary from individual to individual. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Between 1 and 3 doses may be administered for a 1-36 week period. Preferably, 3 doses are administered, at intervals of 3-4 months, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of polypeptide or polynucleotide that, when administered as described above, is capable of raising an immune response in an immunized patient sufficient to protect the patient from *B. microti* infection for at least 1-2 years. In general, the amount of polypeptide present in a dose (or produced *in situ* by the polynucleotide in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg, and preferably from about 100 pg to about 1 μg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed.

Biodegradable microspheres (*e.g.*, polylactic galactide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Any of a variety of adjuvants may be employed in the vaccines of this invention to nonspecifically enhance the immune response. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a nonspecific stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis*. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Freund's Complete Adjuvant (Difco Laboratories, Detroit, MI) and Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ). Other suitable adjuvants include alum, biodegradable microspheres, monophosphoryl lipid A and quil A.

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1

ISOLATION OF DNA SEQUENCES ENCODING *B. MICROTI* ANTIGENS

This example illustrates the preparation of DNA sequences encoding *B. microti* antigens by screening a *B. microti* expression library with sera obtained from patients infected with *B. microti*.

B. microti genomic DNA was isolated from infected hamsters and sheared by sonication. The resulting randomly sheared DNA was used to construct a *B. microti* genomic expression library (approximately 0.5 - 4.0 kbp inserts) with *Eco*RI adaptors and a Lambda ZAP II/*Eco*RI/CIAP vector (Stratagene, La Jolla, CA). The unamplified library (1.2×10^6/ml) was screened with an *E. coli* lysate-absorbed *B. microti* patient serum pool, as described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. Positive plaques were visualized and purified with goat-anti-human alkaline phosphatase. Phagemid from the plaques was rescued and DNA sequence for positive

clones was obtained using forward, reverse, and specific internal primers on a Perkin Elmer/Applied Biosystems Inc. Automated Sequencer Model 373A (Foster City, CA).

Seventeen antigens (hereinafter referred to as BMNI-1 - BMNI-17) were purified and three were possibly redundant. The determined DNA sequences for BMNI-1 - BMNI-17 are shown in SEQ ID NO: 1-17, respectively. The deduced amino acid sequences for BMNI-1 - BMNI-6, BMNI-8 and BMNI-10 - BMNI-17 are shown in SEQ ID NO: 18-32, respectively, with the predicted 5' and 3' protein sequences for BMNI-9 being shown in SEQ ID NO: 33 and 34, respectively.

The isolated DNA sequences were compared to known sequences in the gene bank using the DNA STAR system. Nine of the seventeen antigens (BMNI-1, BMNI-2, BMNI-3, BMNI-5, BMNI-6, BMNI-7, BMNI-12, BMNI-13 and BMNI-16) share some homology, with BMNI-1 and BMNI-16 being partial clones of BMNI-3. All of these nine antigens contain a degenerate repeat of six amino acids (SEQ ID NO: 35), with between nine to twenty-two repeats occurring in each antigen. The repeat portion of the sequences was found to bear some similarity to a *Plasmodium falciparum* merozoite surface antigen (MSA-2 gene). Fig. 1 shows the genomic sequence of BMNI-3 including a translation of the putative open reading frame, with the internal six amino acid repeat sequence being indicated by vertical lines within the open reading frame.

A second group of five antigens bear some homology to each other but do not show homology to any previously identified sequences (BMNI-4, BMNI-8, BMNI-9, BMNI-10 and BMNI-11). These antigens may belong to a family of genes or may represent parts of a repetitive sequence. BMNI-17 contains a novel degenerate repeat of 32 amino acids (SEQ ID NO: 36). Similarly, the reverse complement of BMNI-17 (SEQ ID NO: 37) contains an open reading frame that encodes an amino acid sequence (SEQ ID NO: 38) having a degenerate 32 amino acid repeat (SEQ ID NO: 39).

The reverse complement of BMNI-3 (SEQ ID NO: 40) has an open reading frame which shows homology with the BMNI-4-like genes. The predicted amino acid sequence encoded by this open reading frame is shown in SEQ ID NO: 41. The reverse complement of BMNI-5 (SEQ ID NO: 42) contains a partial copy of a

BMNI-3-like sequence and also an open reading frame with some homology to two yeast genes (*S. cerevisiae* G9365 ORF gene, and *S. cerevisiae* accession no. U18922). The predicted 5' and 3' amino acid sequences encoded by this open reading frame are shown in SEQ ID NO: 43 and 44, respectively. The reverse complement of BMNI-7 (SEQ ID NO: 45) contains an open reading frame encoding the amino acid sequence shown in SEQ ID NO: 46.

A telomeric repeat sequence, which is conserved over a wide range of organisms, was found in five antigens (BMNI-2, BMNI-5, BMNI-6, BMNI-7 and BMNI-16), indicating that many of the isolated genes may have a telomere-proximal location in the genome. BMNI-10 appears to include a double insert, the 3'-most segment having some homology to *E. coli* aminopeptidase N. In addition, BMNI-7 contains apparently random insertions of hamster DNA. One such insertion has characteristics of a transposible element (*i.e.* poly A tail and flanked by a direct repeat).

In subsequent studies, two additional *B. microti* antigens were isolated by screening the *B. microti* genomic DNA expression library described above with a serum pool from *B. microti* infected patients that showed low reactivity with recombinant proteins generated from clones BMNI-2 - BMNI-17. The determined DNA sequences for these two clones, hereinafter referred to as MN-10 and BMNI-20, are provided in SEQ ID NO: 50 and 51, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 52 and 53. MN-10 was found to extend the sequence of BMNI-4 in the 3' direction and BMNI-20 was found to extend the sequence of BMNI-17 in the 5' direction.

EXAMPLE 2

SYNTHESIS OF SYNTHETIC POLYPEPTIDES

Polypeptides may be synthesized on a Millipore 9050 peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugating or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray mass spectrometry and by amino acid analysis.

This procedure was used to synthesize two peptides (hereinafter referred to as BABS-1 and BABS-4) made to the repeat region of the isolated *B. microti* antigen BMNI-3. The sequences of BABS-1 and BABS-4 are shown in SEQ ID NO: 47 and 48, respectively.

EXAMPLE 3

USE OF REPRESENTATIVE ANTIGENS AND PEPTIDES FOR SERODIAGNOSIS OF *B. MICROTI* INFECTION

A. Diagnostic Properties of Representative Antigens and Peptides as determined by ELISA

The diagnostic properties of recombinant BMNI-3, BMNI-4, BMNI-6, BMNI-15, MN-10 and BMNI-20, and the BABS-1 and BABS-4 peptides were determined as follows.

Assays were performed in 96 well plates coated overnight at 4 °C with 200 ng antigen/well added in 50 µl of carbonate coating buffer. The plate contents were then removed and the wells were blocked for 2 hours with 200 µl of PBS/1% BSA. After the blocking step, the wells were washed six times with PBS/0.1% Tween 20™. Fifty microliters of sera, diluted 1:100 in PBS/0.1% Tween 20™/0.1% BSA, was then added to each well and incubated for 30 minutes at room temperature. The plates were then washed six times with PBS/0.1 % Tween 20™.

The enzyme conjugate (horseradish peroxidase-Protein A, Zymed, San Francisco, CA) was then diluted 1:20,000 in PBS/0.1% Tween 20™/0.1% BSA, and 50 µl of the diluted conjugate was added to each well and incubated for 30 minutes at room temperature. Following incubation, the wells were washed six times with PBS/0.1% Tween 20™. 100 µl of tetramethylbenzidine peroxidase substrate (Kirkegaard and Perry Laboratories, Gaithersburg, MD) was added, undiluted, and incubated for 15 minutes. The reaction was stopped by the addition of 100 µl of 1N H_2SO_4 to each well and the plates were read at 450 nm.

Fig. 2a shows the reactivity of the recombinant BMNI-3 and BMNI-6 antigens and the two peptides BABS-1 and BABS-4 in the ELISA assay. The recombinant antigens and the two peptides were negative in ELISA with all seven samples from normal (*B. microti* negative) individuals. In contrast, both BMNI-3 and BMNI-6 detected six of the nine *B. microti*-infected samples, as compared to two out of the nine for the BABS-1 and BABS-4 peptides. This would suggest that BMNI-3 and BMNI-6 may contain other antigenic epitopes in addition to those present in the repeat

epitopes in BABS-1 and BABS-4, or that an insufficient number of repeats are available in the peptides to fully express the antigenic epitopes present in the recombinant antigens BMNI-3 and BMNI-6.

Fig. 2b shows the ELISA reactivity of the recombinant antigens BMNI-4 and BMNI-15. Both recombinants were negative with all fifteen samples from normal individuals. BMNI-4 detected four out of nine *B. microti*-infected samples and BMNI-15 detected six out of nine *B. microti*-infected samples. Both BMNI-4 and BMNI-15 detected a *B. microti*-infected sample which was not detected by BMNI-3 or BMNI-6, suggesting that BMNI-4 and BMNI-15 might be complementary to BMNI-3 and BMNI-6 in the ELISA test described herein.

The ELISA reactivity of recombinant MN-10 and BMNI-20 with sera from *B. microti*-infected patients and from normal donors is shown in Fig. 3. MN-10 and BMNI-20 were found to be reactive with *B. microti*-infected sera that were not reactive with recombinant BMNI-2 through BMNI-17. Therefore, MN-10 and BMNI-20 may be usefully employed in combination with other *B. microti* antigens of the present invention for the detection of *B. microti* infection.

Table 1 shows the reactivity of the recombinant *B. microti* antigens BMNI-2, BMNI-17, MN-10 and a combination of BMNI-17 and MN-10, as determined by ELISA, with *Babesia*-positive sera, sera positive for both *Babesia* and *Ehrlichia*, sera positive only for *Ehrlichia*, Lyme disease sera and sera from normal donors. The data indicate a sensitivity of approximately 93% and a specificity in normal donors in excess of 98%. These results indicate that a combination of BMNI-17 and MN-10 is particularly effective in the diagnosis of *B. microti* infection.

TABLE 1

Antigen	*Babesia*	*Babesia/Ehrlichia*	*Ehrlichia*	Lyme	Normal donors
BMNI-2	27/50	2/3	1/4	0/10	1/73
BMNI-17	35/50	3/3	0/4	0/10	0/86
MN-10	37/49	3/3	0/4	1/10	1/98
BMNI-17/ MN-10	46/50	3/3	0/4	1/10	1/98

B. Diagnostic Properties of Representative Antigens and Peptides as determined by Western Analysis

Western blot analyses were performed on representative *B. microti* antigens as follows.

Antigens were induced as pBluescript SK- constructs (Stratagene), with 2 mM IPTG for three hours (T3), after which the resulting proteins from time 0 (T0) and T3 were separated by SDS-PAGE on 15% gels. Separated proteins were then transferred to nitrocellulose and blocked for 1 hr in 0.1% Tween 20™/PBS. Blots were then washed 3 times in 0.1% Tween 20™/PBS and incubated with a *B. microti* patient serum pool (1:200) for a period of 2 hours. After washing blots in 0.1% Tween 20™/PBS 3 times, immunocomplexes were detected by the addition of Protein A conjugated to ^{125}I (1/25000; NEN-Dupont, Billerica, MA) followed by exposure to X-ray film (Kodak XAR 5; Eastman Kodak Co., Rochester, NY) at -70 °C for 1 day.

As shown in Fig. 4, resulting bands of reactivity with serum antibody were seen at 43 kDa for BMNI-1, 38 kDa for BMNI-2, 45 kDa for BMNI-3, 37 kDa for BMNI-4, 18 and 20 kDa for BMNI-5, 35 and 43 kDa for BMNI-7, 32 kDa for BMNI-9, 38 kDa for BMNI-11, 30 kDa for BMNI-12, 45 kDa for BMNI-15, and 43 kDa for BMNI-17 (not shown). Antigen BMNI-6, after reengineering as a pET 17b construct (Novagen, Madison, WI) showed a band of reactivity at 33 kDa (data not shown). Protein size standards, in kDa (Gibco BRL, Gaithersburg, MB), are shown to the left of the blots.

Western blots were performed on purified BMNI-3, BMNI-2, BMNI-15, BMNI-17 and MN-10 recombinant antigen with a series of patient sera from *B. microti* patients and from patients with either Lyme disease or ehrlichiosis. Specifically, purified recombinant antigen (4 μg) was separated by SDS-PAGE on 12% gels. Protein was then transferred to nitrocellulose membrane for immunoblot analysis. The membrane was first blocked with PBS containing 1% Tween 20™ for 2 hours. Membranes were then cut into strips and incubated with individual sera (1/500) for two hours. The strips were washed 3 times in PBS/0.1% Tween 20™ containing 0.5 M NaCl prior to incubating with Protein A-horseradish peroxidase conjugate (1/20,000) in PBS/0.1% Tween 20™/0.5 M NaCl for 45 minutes. After further washing three times

in PBS/0.1% Tween 20™/0.5 M NaCl, ECL chemiluminescent substrate (Amersham, Arlington Heights, IL) was added for 1 min. Strips were then reassembled and exposed to Hyperfilm ECL (Amersham) for 5-30 seconds.

Lanes 1-9 of Fig. 5 show the reactivity of purified recombinant BMNI-3 with sera from nine *B. microti*-infected patients, of which five were clearly positive and a further two were low positives detectable at higher exposure to the hyperfilm ECL. This correlates with the reactivity as determined by ELISA. In contrast, no immunoreactivity was seen with sera from patients with either ehrlichiosis (lanes 10 and 11) or Lyme disease (lanes 12-14), or with sera from normal individuals (lanes 15-20). A major reactive band appeared at 45 kDa and a small break down band was seen at approximately 25 kDa.

Table 2, below, summarizes the reactivity of the recombinant antigens BMNI-2, BMNI-15, BMNI-17 and MN-10 with *B. microti* positive sera. No reactivity was seen with Lyme or *Ehrlichia*-infected sera, with little or no reactivity being seen with normal sera.

TABLE 2

Sample ID	BMNI-2	BMNI-15	BMNI-17	MN-10
BM8	++	++	+++++	-
BM21	++	-	++++	++++
COR4	±	++++	++++	+
COR5	±	+++	+	-
252	++++	++++	++++++	+++

- indicates no reactivity

EXAMPLE 4

ANALYSIS OF GEOGRAPHIC VARIATION WITHIN ANTIGENS

The reactivity of the inventive antigens with sera from *B. microti* patients, as determined by Western blot, was found to vary with the U.S. location of the patients. Accordingly, geographic variation within the gene encoding the exemplary antigen BMNI-6 was examined as follows.

Two PCR primers, referred to as BMNI-6/5' and BMNI-6/3' (SEQ ID NOS: 54 and 55, respectively) were designed based on the region flanking the six amino acid degenerate repeat region of BMNI-6 (SEQ ID NO: 6). These primers were employed to amplify genomic DNA from whole blood obtained from twelve *B. microti*-infected patients and genomic DNA from whole blood from *P. leucopus* and hamsters in a Perkin Elmer 480 thermal cycler using the manufacturer's protocol. PCR products were evaluated for size on 2% agarose gels and then Southern blotted and probed with a DIG-labeled oligonucleotide. Positive clones were sequenced using an Applied Biosystems Model 373A or 377 sequencer. RT-PCR was performed on Trizol LS extracted *B. microti*-infected hamster whole blood RNA using the primers described above, and the resulting clones were sequenced as described above.

These studies resulted in the isolation of twelve BMNI-6 homologues, referred to hereinafter as BI254, BI1053, BI2227, BI2259, BI2253, BI2018, RIFS, MN1HAM, MN2, MN1PAT, MN3 and MRT with MN1HAM being obtained from hamster and the other eleven from patients. The determined DNA sequences of these clones are provided in SEQ ID NO: 56-67, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 68-79, respectively. Isolates from hamsters had the same sequences as found in the corresponding human blood, suggesting that genetic variation of BMNI-6 does not occur during passage. However, clones from different patients often showed variation in the number and location of the degenerate repeat found within BMNI-6. An alignment of the repeat regions from each of the twelve clones is provided in Figure 6. Furthermore, strains that were closely related geographically were also closely related at the sequence level. For example, three patients from Nantucket Island, MA, harbored clones (BI2253, BI2259 and BI2227) that were indistinguishable from each other but distinct from those

found in other northeastern or upper midwestern strains. These results suggest that considerable antigenic diversity exists among isolates of *B. microti* from the U.S. and that geographic clustering of subtypes exists.

EXAMPLE 5

PREPARATION AND CHARACTERIZATION OF *B. MICROTI* FUSION PROTEINS

A. PREPARATION OF A FUSION PROTEIN CONTAINING MN-10 AND BMNI-17

A fusion protein containing the *B. microti* antigens MN-10 and BMNI-17, referred to as BaF-3, was prepared as follows.

MN-10 and BMNI-17 DNA was used to perform PCR using the primers PDM-285 and PDM-286 (SEQ ID NO: 80 and 81); and PDM-283 and PDM-284 (SEQ ID NO: 82 and 83), respectively. In both cases, the DNA amplification was performed using 10 µl of 10x Pfu buffer (Stratagene), 1 µl of 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 50 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 59°C for 15 sec and 72°C for 3 min, and lastly by 72°C for 4 min. The MN-10 and BMNI-17 PCR products were digested with SspI and then ligated using a ligation kit from Panvera (Madison, WI). The resulting BaF-3 fusion was PCR amplified using primers PDM 285 and PDM-284 and the same conditions as listed above. This PCR product was then digested with ScaI and EcoRI, and cloned into a modified pET28 vector. The fusion construct was confirmed by sequencing. The expression construct was transformed into BL21 (DE3) CodonPlus cells (Novagen, Madison, WI) for induction and expression. The protein came out in the inclusion body pellet. This pellet was washed three times with a 0.5% CHAPS wash in 20 mM Tris (8.0) and 300 mM NaCl. The pellet was then solubilized in 8 M urea, 20 mM Tris (8.0), 300 mM NaCl and batch bound to Nickel NTA resin (Qiagen). The nickel resin was washed with 100 ml 8 M urea, 20 mM Tris (9.0), 300 mM NaCl, 1% DOC. A second wash was performed as described for the first wash, but with the omission of DOC. The protein was first eluted with 8 M urea, 20 mM Tris (9.0), 100 mM NaCl and 500 mM imidazole. In a second elution, the imidazole was increased to 1 M. The elutions were run on a 4-20 SDS-PAGE gel and the fractions containing the protein of interest were pooled and dialyzed against 1 mM Tris (8.).

The determined cDNA sequence of coding region for the BaF-3 fusion protein is provided in SEQ ID NO: 84, with the corresponding amino acid sequence being provided in SEQ ID NO: 85.

B. PREPARATION OF A FUSION PROTEIN CONTAINING BMNI-15, MN-10 and BMNI-17

A fusion protein containing the *B. microti* antigens BMNI-15, MN-10 and BMNI-17, referred to as BaF-4, was prepared as follows.

BMNI-15 DNA was used to perform PCR using the primers PDM-349 and PDM-363 (SEQ ID NO: 88 and 89). DNA amplification was performed using 10 µl of 10x Pfu buffer (Stratagene), 1 µl of 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 50 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 61°C for 15 sec and 72°C for 3 min, and lastly by one cycle of 72°C for 4 min. The PCR product was digested with PvuII and EcoRI, and cloned into a modified pET28 vector, which had been cut with Eco72I and EcoRI. The construct was confirmed to be correct by sequencing. MN-10/BMNI-17 DNA from BaF-3, described above, was used to perform PCR using the primers PDM-364 and PDM-284 (SEQ ID NO: 90 and 83, respectively). DNA amplification was performed using 10 µl of 10x Pfu buffer (Stratagene), 1 µl of 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 50 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 60°C for 15 sec and 72° C for 6 min, and lastly by 72°C for 4 min. The PCR product was cut with BamHI and EcoRI, and cloned into the pPDM BMNI-15 construct at the BamHI and EcoRI sites. The resulting construct was found by sequence analysis to have a single base pair deletion 419 bp in from the stop codon. This base pair deletion was corrected by digesting the pPDM BaF4B-6 clone with KpnI and SphI, and purifying the 2.6 kb insert plus 5' vector. This band was then cloned into pPDM Trx2H BaF3-10 that was digested with the same enzymes and contained the 3' end of BMNI-17 plus most of the pPDM vector. The correct sequence was confirmed by sequence analysis and then transformed into the BL21 CodonPlus expression host (Novagen).

The determined cDNA sequence of the coding region of the BaF-4 fusion protein is provided in SEQ ID NO: 86, with the corresponding amino acid sequence being provided in SEQ ID NO: 87.

One of skill in the art will appreciate that the order of the individual antigens within the fusion protein may be changed and that comparable or enhanced activity could be expected provided each of the epitopes is still functionally available. In addition, truncated forms of the proteins containing active epitopes may be used in the construction of fusion proteins.

Although the present invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, changes and modifications can be carried out without departing from the scope of the invention which is intended to be limited only by the scope of the appended claims.

CLAIMS

1. An isolated polypeptide comprising an immunogenic portion of a *B. microti* antigen or a variant thereof, wherein said antigen comprises an amino acid sequence encoded by a DNA sequence selected from the group consisting of: (a) sequences recited in SEQ ID NO: 1-17, 37, 40, 42, 45, 50 and 51; (b) the complements of said sequences; and (c) DNA sequences that hybridize to a sequence of (a) or (b) under moderately stringent conditions.

2. An isolated antigenic epitope of a *B. microti* antigen comprising the amino acid sequence -X_1-X_2-X_3-X_4-X_5-Ser-, wherein X_1 is Glu or Gly, X_2 is Ala or Thr, X_3 is Gly or Val, X_4 is Trp or Gly and X_5 is Pro or Ser.

3. An isolated antigenic epitope according to claim 2 wherein X_1 is Glu, X_2 is Ala and X_3 is Gly.

4. An isolated antigenic epitope according to claim 2 wherein X_1 is Gly, X_2 is Thr and X_5 is Pro.

5. An isolated polypeptide comprising at least two contiguous antigenic epitopes according to claim 2.

6. An isolated antigenic epitope of a *B. microti* antigen comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 36 and 39.

7. An isolated polypeptide comprising at least two contiguous antigenic epitopes according to claim 6.

8. An isolated polynucleotide comprising a DNA sequence encoding a polypeptide according to any one of claims 1, 5 and 7.

9. A recombinant expression vector comprising a polynucleotide

according to claim 8.

10. A host cell transformed with an expression vector according to claim 9.

11. The host cell of claim 10 wherein the host cell is selected from the group consisting of *E. coli*, yeast and mammalian cells.

12. A fusion protein comprising at least two polypeptides according to any one of claims 1, 5 and 7.

13. A fusion protein comprising a polypeptide having an amino acid sequence of SEQ ID NO: 32.

14. The fusion protein of claim 13 further comprising a polypeptide having an amino acid sequence of SEQ ID NO: 52.

15. A fusion protein comprising two or more antigenic epitopes according to claims 2 or 6.

16. A fusion protein comprising at least one polypeptide according to any one of claims 1, 5 and 7, and at least one antigenic epitope according to any one of claims 2 and 6.

17. A method for detecting *B. microti* infection in a patient, comprising:

(a) obtaining a sample from the patient;

(b) contacting the sample with at least one polypeptide comprising an immunogenic portion of a *B. microti* antigen; and

(c) detecting the presence of antibodies that bind to the polypeptide.

18. A method for detecting *B. microti* infection in a patient, comprising:

(a) obtaining a sample from the patient;

(b) contacting the sample with at least one antigenic epitope according to any one of claims 2 and 6; and

(c) detecting the presence of antibodies that bind to the antigenic epitope.

19. The method of claim 18 wherein the antigenic epitope is bound to a solid support.

20. The method of claim 19 wherein the solid support comprises nitrocellulose, latex or a plastic material.

21. A method for detecting *B. microti* infection in a patient, comprising:

(a) obtaining a sample from the patient;

(b) contacting the sample with at least one polypeptide according to any one of claims 1, 5 and 7; and

(c) detecting the presence of antibodies that bind to the polypeptide.

22. A method for detecting *B. microti* infection in a patient, comprising:

(a) obtaining a sample from the patient;

(b) contacting the sample with at least one polypeptide according to any one of claims 1, 5 and 7, and at least one antigenic epitope according to any one of claims 2 and 6; and

(c) detecting the presence of antibodies that bind to the polypeptide or antigenic epitope.

23. A method for detecting *B. microti* infection in a patient, comprising:

(a) obtaining a sample from the patient;

(b) contacting the sample with a fusion protein according to any one of claims 12-16 and 67; and

(c) detecting the presence of antibodies that bind to the fusion protein.

24. The method of claims 17, 18, 21, 22 or 23 wherein the biological sample is selected from the group consisting of whole blood, serum, plasma, saliva, cerebrospinal fluid and urine.

25. The method of claim 24 wherein the biological sample is whole blood.

26. A method for detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the sample with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotide primers is specific for a DNA molecule according to claim 8; and

(b) detecting in the sample a DNA sequence that amplifies in the presence of the first and second oligonucleotide primers.

27. The method of claim 26 wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a DNA molecule according to claim 8.

28. A method for detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the sample with one or more oligonucleotide probes specific for a DNA molecule according to claim 8; and

(b) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe.

29. The method of claim 28 wherein the probe comprises at least about 15 contiguous nucleotides of a DNA molecule according to claim 8.

30. The method of claims 26 or 28 wherein the biological sample is selected from the group consisting of whole blood, sputum, serum, plasma, saliva, cerebrospinal fluid and urine.

31. A method for detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the biological sample with a binding agent which is capable of binding to a polypeptide comprising an immunogenic portion of a *B. microti* antigen; and

(b) detecting in the sample a polypeptide that binds to the binding agent, thereby detecting *B. microti* infection in the biological sample.

32. A method for detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the biological sample with a binding agent which is capable of binding to a polypeptide according to any one of claims 1, 5 and 7; and

(b) detecting in the sample a polypeptide that binds to the binding agent, thereby detecting *B. microti* infection in the biological sample.

33. A method of detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the biological sample with a binding agent which is capable of binding to an antigenic epitope according to any one of claims 2 and 6; and

(b) detecting in the sample an antigenic epitope that binds to the binding agent, thereby detecting *B. microti* infection in the biological sample.

34. A method of detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the biological sample with a first binding agent which is capable of binding to a polypeptide according to any one of claims 1, 5 and 7, and a second binding agent which is capable of binding to an antigenic epitope according to any one of claims 2 and 6; and

(b) detecting in the sample a polypeptide that binds to the first binding agent or an antigenic epitope that binds to the second binding agent, thereby detecting *B. microti* infection in the biological sample.

35. A method of detecting *B. microti* infection in a biological sample, comprising:

(a) contacting the biological sample with a binding agent which is capable of binding to a fusion protein according to any one of claims 12-16 and 67; and

(b) detecting in the sample a polypeptide that binds to the binding agent, thereby detecting *B. microti* infection in the biological sample.

36. The method of claims 32, 33, 34 or 35 wherein the binding agent is a monoclonal antibody.

37. The method of claims 32, 33, 34 or 35 wherein the binding agent is a polyclonal antibody.

38. A diagnostic kit comprising:

(a) at least one polypeptide comprising an immunogenic portion of a *B. microti* antigen; and

(b) a detection reagent.

39. A diagnostic kit comprising

(a) at least one polypeptide according to any one of claims 1, 5 and 7; and

(b) a detection reagent.

40. The kit of any one of claims 38 and 39 wherein the polypeptide is immobilized on a solid support.

41. The kit of claim 40 wherein the solid support is selected from the group consisting of nitrocellulose, latex, and plastic materials.

42. A diagnostic kit comprising:

(a) at least one antigenic epitope according to any one of claims 2 and 6; and

(b) a detection reagent.

43. The kit of claim 42 wherein the antigenic epitope is immobilized on a solid support.

44. The kit of claim 43 wherein the solid support is selected from the group consisting of nitrocellulose, latex, and plastic materials.

45. A diagnostic kit comprising:

(a) at least one antigenic epitope according to any one of claims 2 and 6;

(b) at least one polypeptide according to any one of claims 1, 5 and 7; and

(c) a detection reagent.

46. A diagnostic kit comprising:

(a) at least one fusion protein according to any one of claims 12-16 and 67; and

(b) a detection reagent.

47. The kit of any one of claims 38, 39, 42, 45 and 46 wherein the detection reagent comprises a reporter group conjugated to a binding agent.

48. The kit of claim 47 wherein the binding agent is selected from the group consisting of anti-immunoglobulins, Protein G, Protein A and lectins.

49. The kit of claim 47 wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

50. A diagnostic kit comprising at least one polymerase chain reaction primer, the primer being specific for a DNA molecule according to claim 8.

51. The kit of claim 50 wherein the polymerase chain reaction primer comprises at least about 10 contiguous nucleotides of a DNA molecule according to claim 8.

52. A diagnostic kit comprising at least one oligonucleotide probe, the oligonucleotide probe being specific for a DNA molecule according to claim 8.

53. The kit of claim 52 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a DNA molecule according to claim 8.

54. A monoclonal antibody that binds to a polypeptide according to any one of claims 1, 5 and 7.

55. A monoclonal antibody that binds to an antigenic epitope according to any one of claims 2 and 6.

56. A polyclonal antibody that binds to a polypeptide according to any one of claims 1, 5 and 7.

57. A polyclonal antibody that binds to an antigenic epitope according to any one of claims 2 and 6.

58. A pharmaceutical composition comprising at least one polypeptide according to any one of claims 1, 5 and 7, and a physiologically acceptable carrier.

59. A pharmaceutical composition comprising at least one DNA molecule according to claim 8 and a physiologically acceptable carrier.

60. A pharmaceutical composition comprising at least one antigenic epitope according to any one of claims 2 and 6, and a physiologically acceptable carrier.

61. A vaccine comprising at least one polypeptide according to any one of claims 1, 5 and 7, and a non-specific immune response enhancer.

62. A vaccine comprising at least one DNA molecule according to claim 8 and a non-specific immune response enhancer.

63. A vaccine comprising at least one antigenic epitope according to any one of claims 2 and 6, and a non-specific immune response enhancer.

64. The vaccine of any one of claims 61-63 wherein the non-specific immune response enhancer is an adjuvant.

65. A method for inducing protective immunity in a patient, comprising administering to a patient a pharmaceutical composition according to any

one of claims 58-60.

66. A method for inducing protective immunity in a patient, comprising administering to a patient a vaccine according to any one of claims 61-63.

67. A fusion protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 85 and 87.

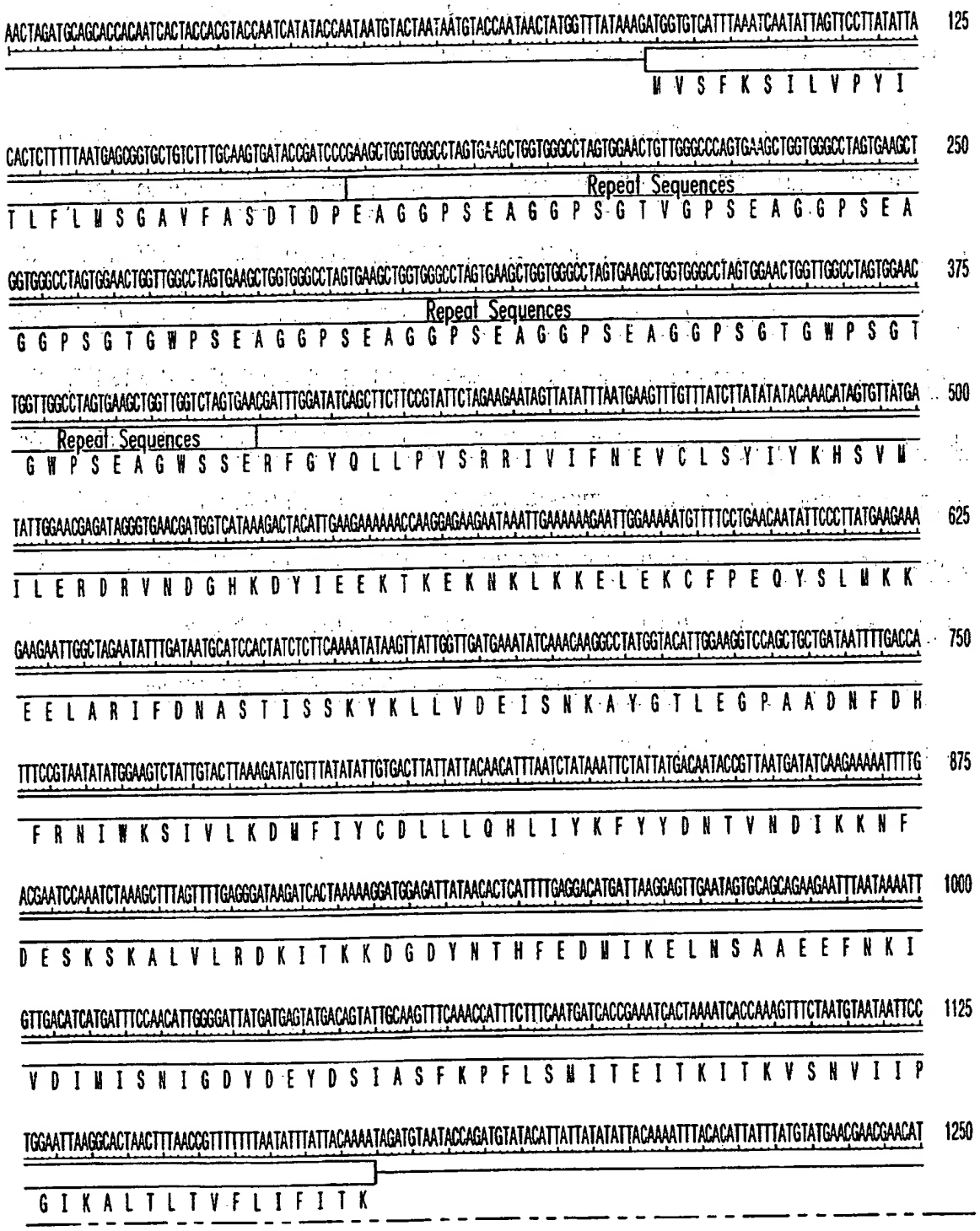

Fig. 1A

RECTIFIED SHEET

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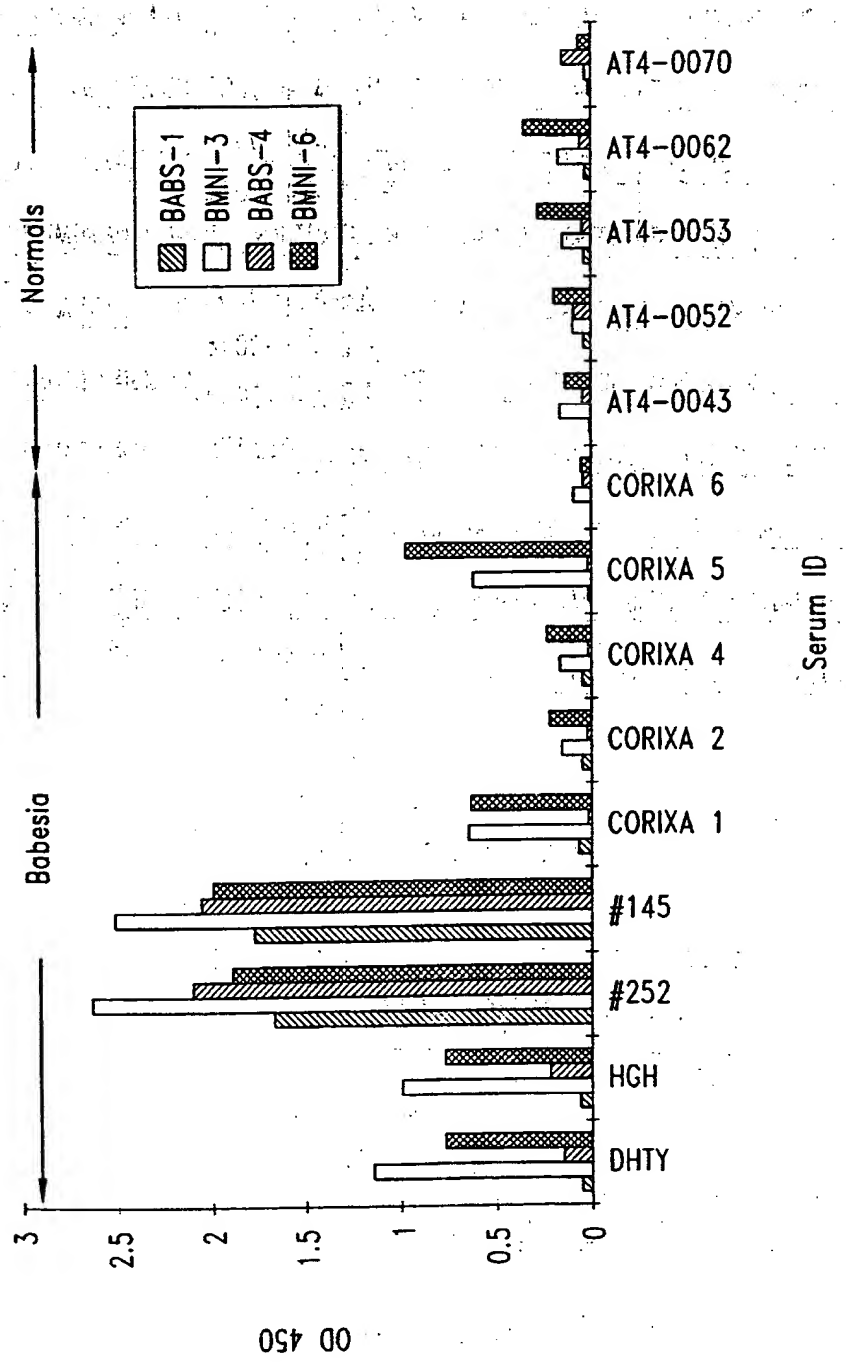
Fig. 1B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BABS-4
BMNI-6
Normals
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AT4-0052
AT4-0043
CORIXA 6
CORIXA 5
CORIXA 4
CORIXA 2
CORIXA 1
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#252
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DHTY
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2
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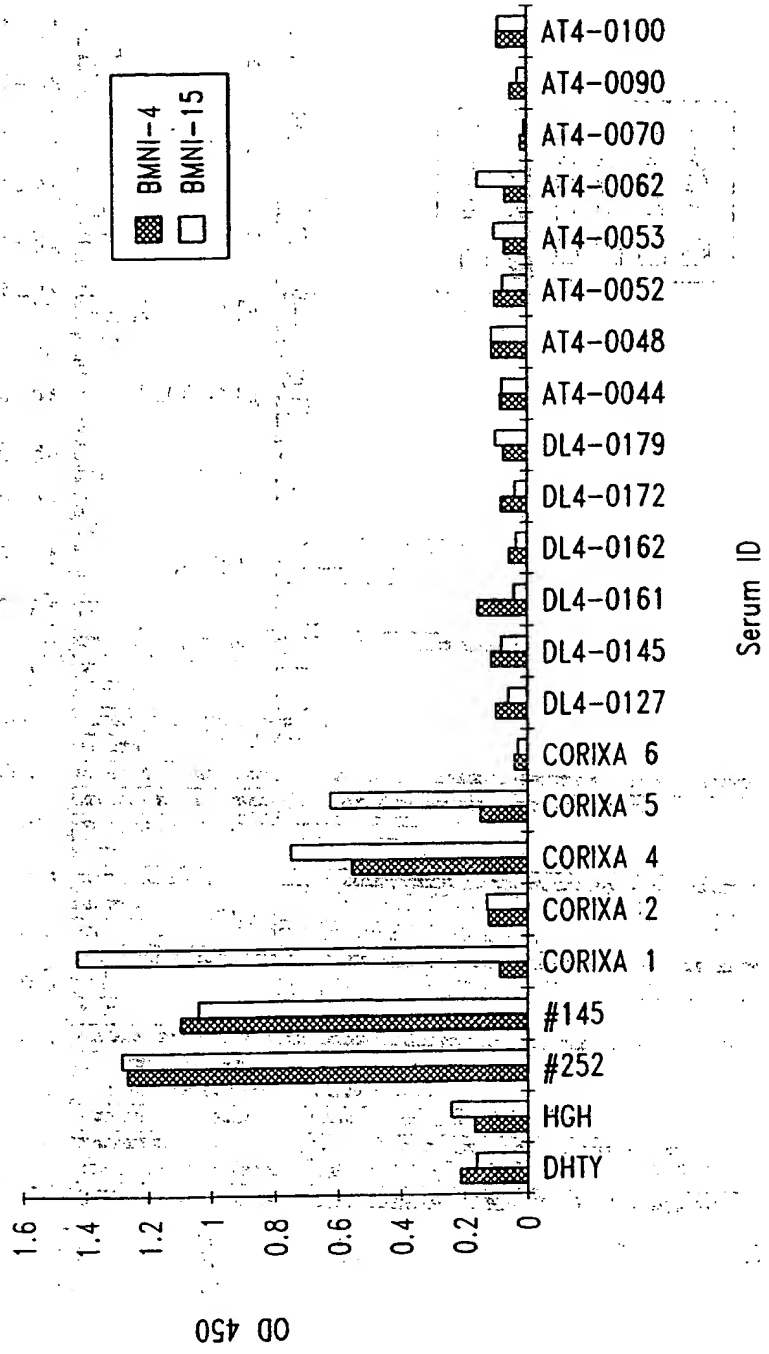
0
OD 450

Fig. 2A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CORIXA 4
CORIXA 2
CORIXA 1
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#252
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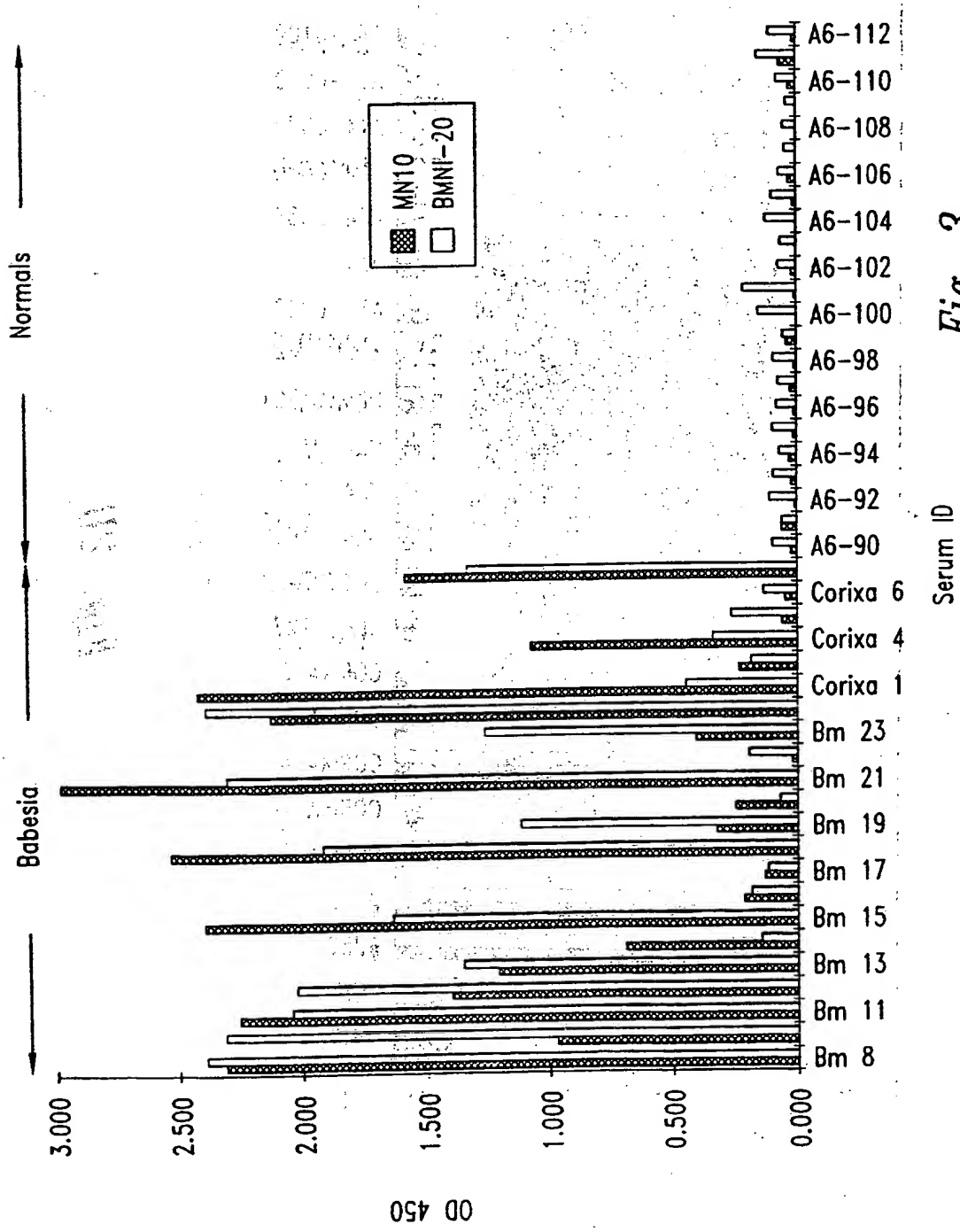
0
OD 450

Fig. 2B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A6-96
A6-94
A6-92
A6-90
Corixa 6
Corixa 4
Corixa 1
Bm 23
Bm 21
Bm 19
Bm 17
Bm 15
Bm 13
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Serum ID
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1.000
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OD 450

Fig. 3

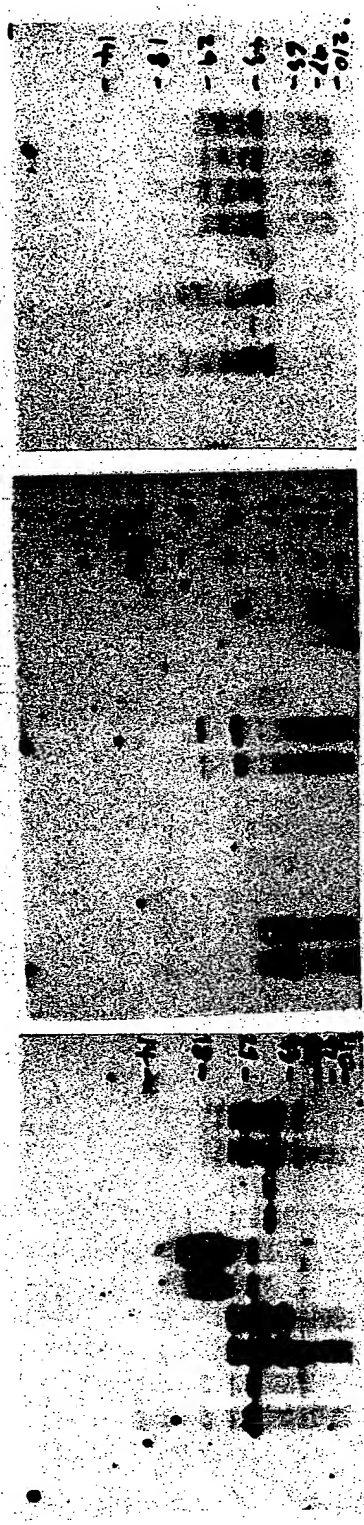
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Fig. 4

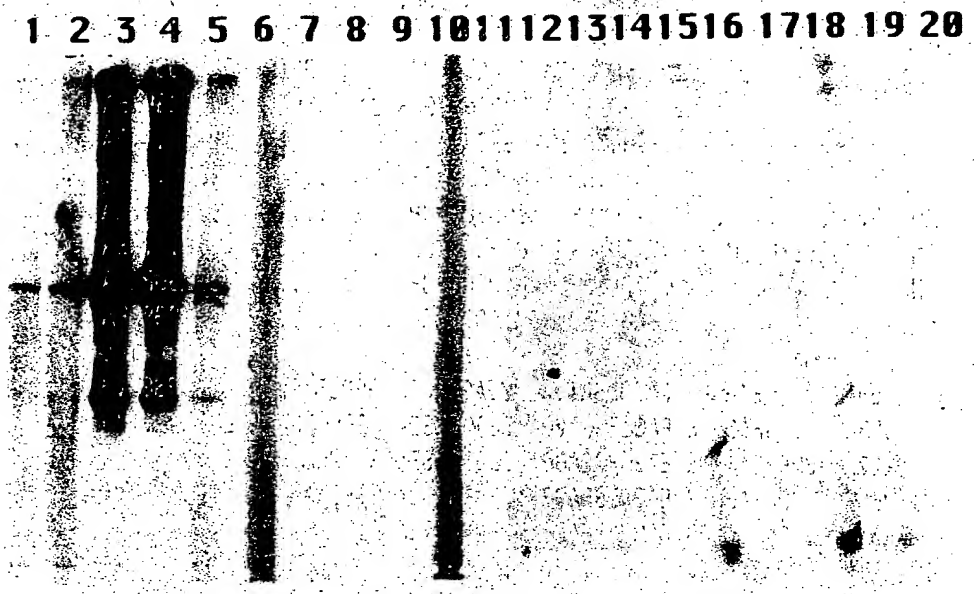

Fig. 5

```
BI254     ..........  ..AGDTDREA GGPSGTVGP.  ..........  ..........
BI1053    ..........  ...GDTDREA GGPSGTVGP.  ..........  ..........
BI2227    ..........  ..AGDTDREA GGPSGTVGP.  ..........  .SEAGGPSEA
BI2259    ..........  ..AGDTDREA GGPSGTVGP.  ..........  .SEAGGPSEA
BI2253    ..........  .........EA GGPSGTVGP.  ..........  .SEAGGPSEA
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Fig. 6A

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Fig. 6B

SEQUENCE LISTING

<110> Corixa Corporation et al.

<120> COMPOUNDS AND METHODS FOR THE DIAGNOSIS AND TREATMENT OF B. MICROTI INFECTION

<130> 210121.42602PC

<140> PCT
<141> 2000-04-05

<160> 90

<170> FastSEQ for Windows Version 3.0

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atatcaatca tacagtatac aattatataa aatattaaca acatataaca accaacatta 1200
atatatacat aatatcttta ttaatcaata tttaatcaat acaataatta atagttaact 1260
aactatacac atagtgtata ctaaatt 1287

<210> 12
<211> 572
<212> DNA
<213> Babesia microti

<400> 12
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atgcacattg atgacaacta gatgcagcac cacaatcact accacgtacc aatcatatac 180
caataatgta ctaataatgt accaataact atggtttata aagatggtgt catttaaatc 240
aatattagtt ccttatatta cactcttttt aatgagcggt gctgtctttg caagtgatac 300
cgatcccgaa gctggtgggc ctagtgaagc tggtgggcct agtgaagctg gtgggcctag 360
tggaactgtt gggcccagtg aagctggtgg gcctagtgaa gctggtgggc ctagtggaac 420
tggttggcct agtgaagctg gtgggcctag tgaagctggt gggcctagtg gaactggttg 480
gcctagtgaa gctggttggt ctagtgaacg atttggatat cagcttcttc cgtattctag 540
aagaatagtt acatttaatg aagtttgttt at 572

<210> 13
<211> 2338
<212> DNA
<213> Babesia microti

<400> 13

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tgacaactag atgcagcacc acaatcacta ccacgtacca atcatatacc aataatgtac 180
taataatgta ccaataacta tggtttataa agatggtgtc atttaaatca atattagttc 240
cttatattac actcttttta atgagcggtg ctgtctttgc aagtgatacc gatcccgaag 300
ctggtgggcc tagtggaact gttgggccca gtgaagctgg tgggcctagt gaagctggtg 360
ggcctagtgg aactggttgg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 420
gtggaactgg ttggcctagt gaagctggtt ggtctagtga acgatttgga tatcagcttc 480
ttccgtattc tagaagaata gttacattta atgaagtttg tttatcttat atatacaaac 540
atagtgttat gatattggaa cgagataggg tgaacgatgg tcataaagac tacattgaag 600
aaaaaaccaa ggagaagaat aaattgaaaa aagaattgga aaaatgtttt cctgaacaat 660
attcccttat gaagaaagaa gaattggcta gaatatttga taatgcatcc actatctctt 720
caaaatataa gttattggtt gatgaaatat caaacaaggc ctatggtaca ttggaaggtc 780
cagctgctga taattttgac catttccgta atatatggaa gtctattgta cttaaagata 840
tgtttatata ttgtgactta ttattacaac atttaatcta taaattctat tatgacaata 900
ccattaatga tatcaagaaa aattttgacg aatccaaatc taaagcttta gttttgaggg 960
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tactggggta gatattataa gttatggata agtaaattta tggcgataga ttccaacaaa 1080
tttgtggtta gtagcgacaa tgattatggc tagtgtgtgg agtacttatg agtgaatgat 1140
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tgcaaatagc atttaaattg acatatattg tgtgtatgtc cacgtttatt gcgtttccat 1260
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tgcccatggg caggtttttt tggcaaggga acgacgtacc ggttttattt gcgtgttaaa 1560
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tggtatgtac atatttatcc agcttgtata cctggttcac tagccctact atgatattca 1740
tagtgatgga atattgttac aatggcgatc tatttaatta tatgtcaaaa catggccaac 1800
tgagtgaaga aagggtatca gagtatacag atatttacat agaattttgt tcgaagtcat 1860
ttgggccatt agaagctgcc acgacaaacg catagcgcac ttggatatta aaccagtaag 1920
gttctatgtt acagaggaga atatattatt ggaccatgaa aacaggtgta aattggcgga 1980
ctttggattc tctgcacaca tagggcattt gtaccgctca aacggagtgc tcatcatcgt 2040
ggcacgcatg gtaacacgca attwatggca gattattggt ctccggagca gtgtgccaaa 2100
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ggcatattgg cagttgaatt gtttattgga taccctccat ttggatctac tactgaagag 2220
cccaacaatg tgattatgaa cagaatccac acttaccact ggaccaaaca tgtactttta 2280
tctattacgc agatttttga aatgaagagg gaaaaacatc tactctcgtc gacgcctg 2338

<210> 14
<211> 729
<212> DNA
<213> Babesia microti

<400> 14
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cacttggaag aatttcacca attgcatatg aaacatggaa tccaagagac caaaatttaa 120
aaccttgaaa tagaagcact tatgccaata ttggaaatta cttagtgaag tgatccaaag 180
tactgatttg gtcagaagac atcaccaggg cactagctgg cctagtgacc tgagtatttg 240
tgaaagctga ttttaatgtt gagaacatga aggaagcagt attgaggtaa tggaatcttg 300
tagattatag tagaagccaa ctgagaccaa gaaatgtacg gtaggaatga aataaggtct 360
tgggtggtca ttgcatggag ctgtgaaagt gaagcgttgt tggggtatag attcgcaagt 420
cttggggcat gactatgtgg ggttaccaag gttaggttaa ctgaggtgga aagatccact 480
ctaaatgggg gagttaccat ttcatgtgct gggatcccag agatgtcaaa ggagaaaata 540

agctattgaa taagagcatc tatatcccct gcttcttggc tatggatgtt atgtgactag 600
tcatctctta gtcttacctt caccattata acaagatttt ctagaacttt gggttaaatt 660
aaatccttta ttcctcacgt tgctgtctta gttactttcc tgttgctttg ataaagcatt 720
ctggccaag 729

<210> 15
<211> 1448
<212> DNA
<213> Babesia microti

<400> 15
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gcataattca ctcgattacg gtagaaaagg cgattaactc tgaagatttt gacggaatac 120
aaacactttt acaagtgtct atcattgcta gttacggtcc atctggcgat tacagtagtt 180
ttgtgttcac tccagttgta acagcagaca ccaacgtttt ttacaaatta gagacggatt 240
tcaaacttga tgttgatgtt attactaaga catcactaga attgcccaca agtgttcctg 300
gctttcacta caccgaaact atttaccaag gcacagaatt gtcaaaattt agcaagcctc 360
agtgcaaact taacgatcct cctattacaa caggatcggg gttgcaaata atacatgatg 420
gtttgaataa ttcgacaatt ataaccaaca aagaagttaa tgtggatgga acagatttag 480
ttttttttga attgctccct ccatcggatg gcattcccac cttgcgatca aaattatttc 540
ccgtcctgaa atcaattcca atgatatcta ccggggttaa tgaattactg ttggaagtac 600
tcgagaaccc ctctttccct agtgcaatta gcaattacac cggactgaca ggccgactta 660
acaaattact tacagtttta gacggtattg ttgatagcgc cattagtgtc aagactacag 720
aaactgtccc tgacgacgca gaaacttcta tttcttcatt gaaatcattg ataaaggcaa 780
tacgagataa tattactacc actcgaaacg aagttaccaa agatgatgtt tatgcattga 840
agaaggccct cacttgtcta acgacacacc taatatatca ttcaaaagta gatggtatat 900
cattcgacat gctgggaaca caaaaaaata aatctagccc actaggcaag atcggaacgt 960
ctatggacga tattatagcc atgttttcga atcccaatat gtatcttgtg aaggtggcgt 1020
acttgcaagc cattgaacac atttttctca tatcaaccaa atacaatgat atatttgatt 1080
acaccattga ttttagtaag cgtgaagcta ctgattctgg atcatttacc gatatattgc 1140
tcggaaacaa ggtgaaggaa tctttgtcat ttattgaggg tttgatttct gacataaaat 1200
ctcactcatt gaaagctggg gttacaggag gtatatcaag ttcatcatta tttgatgaaa 1260
tcttcgacga gttaaatttg gatcaagcaa caattagaac ccttgttgca ccattagatt 1320
ggccacttat ctcagacaaa agcctccacc cttcactgaa gatggttgtg gtcctgccag 1380
gatttttcat agttccttaa taacatgaca tttcatagtc ccttcagtcc tgatgacaag 1440
acggtgaa 1448

<210> 16
<211> 1350
<212> DNA
<213> Babesia microti

<400> 16
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tactaactct aagctaagga aatccagcct gctggctatt tacctgcttt cctcgaagtg 120
aaaggccaga gtcaccccca atctttccca aaagattgaa gtcactctct ccatgccggc 180
aaaggtagat ggtgcgaggc tggacatgga tattcataag gtagtagaca attttactct 240
ggatgtagtc ctggactctg ttgaccagaa atctctggcc tacattaatc accttgatga 300
agacagatcc ctaggacaga gtagaaagag caattttatg gtcagaaaat ctgaaactag 360
gagtgtggca agcaaggggg caaggctatc agcacctagt gacaatccca gcacttagaa 420
ggcttagctg gaaggggctt aggtttgacc ctgactcaag acaaatgaac atatgaaaag 480
tatggggaga atgatctgtg tattgactgg tagggcctca tcagctattc cttctctccc 540
tgtcactgcc atctcgtgcc gaattcggca cgagctcgtg ccgaaaccct aaaccctaaa 600
cccctaaacc ctaaacccta aaccctaaac cctaaaccct aaaccctaaa ccctaaaccc 660
taaaccccta aaccccctaaa ccctaaaccc taaaccctaa accctaaacc ctaaacccta 720

aaccctaacc ctaaccctaa ccctaaccct aacctagcct tcattgacgt ctatccccaa 780
tcttagaaga atcttcaaat cgattctaga ataactggaa acaattatca gaaattgtat 840
aactgcttat tagcttatta gcttattagt taggatgtat gcacattgat gacaactaga 900
tgcagcacca caatcactac cacgtaccaa tcatatacca ataatgtact aataatgtac 960
caataactat ggtttataaa gatggtgtca tttaaatcaa tattagttcc ttatattaca 1020
ctctttttaa tgagcggtgc tgtctttgca agtgataccg atcccgaagc tggtgggcct 1080
agtgaagctg gtgggcctag tggaactgtt gggcccagtg aagctggtgg gcctagtgaa 1140
gctggtgggc ctagtggaac tggttggcct agtgaagctg gtgggcctag tgaagctggt 1200
gggcctagtg aagctggtgg gcctagtgaa gctggtgggc ctagtggaac tggttggcct 1260
agtggaactg gttggcctag tgaagctggt tggtctagtg aacgatttgg atatcagctt 1320
cttccgtatt ctagaagaat agttatattt 1350

<210> 17
<211> 1820
<212> DNA
<213> Babesia microti

<400> 17
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aataatgagt ggatgtttca gtcttgaggc tctttaacaa gagtgttgtc ttgtagtcaa 120
agacaaagtg attcgtcatg ccgcattcgc agccaccatc atcatcaggc gacgacgggt 180
ctctttcatt atcctcgggc ttattattgc aaccatgaca ccctttctta caaaagtctt 240
ttttttcag cggtgtctga gtattatgcg attttattcc agccttccca cttttattct 300
tattgagatt gccatgctct tcttcatgag cgtcacttgt ttcctgcggt gtctgagtat 360
catacgattt tattccagca tttccacttt tattcttatt gattttgtca tgccttcttt 420
cacactcttc acatatttct tgcgttgtct gagtatcatg cgatttttctt tcagccttct 480
cacttttatt cgtattgatt ttgtcatgcc cttcttcatg agcgtcactt gtttcctgcg 540
gtgtctgagt atcatacgat tttattccag catttccact tttattctta ttgattttgt 600
catgcccttc ttcacactct tcacatattt cttgcgttgt ctgagtatca tacgatttta 660
ttccagcatt tccacttta ttcttattga ttttgtcatg cccttcttca cactcttcac 720
atatttcttg cgttgtctga gtatcatgcg attttctttc agccttctca cttttattcg 780
tattgggttt gccatgccct tctttacgct cttcatatat ttcttgtgcc gttagtctca 840
gtaagttgtc aagctcttca tatatttctt gcggtgtctg agtatcatgc gattttcttt 900
cagtcttctc acttttattc gtattgagtt tgccattccc ttcttcatga tcgtcacttg 960
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gagctgtatc ttcccagggt ggttgaatta tgtcattctc gccgatttta aatgatggtt 1080
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gctcactatc gcaagcgtct tgtggattga tgttatcatg ttcctggatt tcaacatgta 1260
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accagacagc atcgggtctc tgtgagtttc tattcaggca acaggtgtat tctgtttgcc 1500
agtccaagtg catcctgtat tctagtactg gcttactacc ccaagcaaat cactggcatc 1560
aacatctagc actgagtgaa gcatgatctc ttctacaagg tgtttttcca ttgtgttgta 1620
agcccgtata caaggctgtt cccactcaac aatgaagaga cctcttagca tgaatggcca 1680
gatgtctgtt ctttaaatta aatcaatatg ttttgctcaa tatgtcagac ttgtttgtgg 1740
tggagccaaa attggaggtc ccatcgagat ttggagaaac ttgaaatgaa tgcaaaagat 1800
ggtgggggct actcgtgccg 1820

<210> 18
<211> 263
<212> PRT
<213> Babesia microti

<400> 18
Leu Phe Leu Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp Pro Glu
1 5 10 15
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro
20 25 30
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
35 40 45
Trp Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
50 55 60
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro
65 70 75 80
Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser Ser Glu Arg Phe
85 90 95
Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg Ile Val Ile Phe Asn Glu
100 105 110
Val Cys Leu Ser Tyr Ile Tyr Lys His Ser Val Met Ile Leu Glu Arg
115 120 125
Asp Arg Val Asn Asp Gly His Lys Asp Tyr Ile Glu Glu Lys Thr Lys
130 135 140
Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu Lys Cys Phe Pro Glu Gln
145 150 155 160
Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala Arg Ile Phe Asp Asn Ala
165 170 175
Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu Val Asp Glu Ile Ser Asn
180 185 190
Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala Ala Asp Asn Phe Asp His
195 200 205
Phe Arg Asn Ile Trp Lys Ser Ile Val Leu Lys Asp Met Phe Ile Tyr
210 215 220
Cys Asp Leu Leu Leu Gln His Leu Ile Tyr Lys Phe Tyr Tyr Asp Asn
225 230 235 240
Thr Val Asn Asp Ile Lys Lys Asn Phe Asp Glu Ser Lys Ser Lys Ala
245 250 255
Leu Val Leu Arg Asp Lys Ile
260

<210> 19
<211> 310
<212> PRT
<213> Babesia microti

<400> 19
Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp Pro Glu Ala Gly Gly
1 5 10 15
Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala
20 25 30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
65 70 75 80
Val Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
85 90 95
Gly Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly

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            100                 105                 110
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
        115                 120                 125
Gly Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser Ser
    130                 135                 140
Glu Arg Phe Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg Ile Val Ile
145                 150                 155                 160
Phe Asn Glu Val Cys Leu Ser Tyr Ile Tyr Lys His Ser Val Met Ile
                165                 170                 175
Leu Glu Arg Asp Arg Val Asn Asp Gly His Lys Asp Tyr Ile Glu Glu
            180                 185                 190
Lys Thr Lys Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu Lys Cys Phe
        195                 200                 205
Pro Glu Gln Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala Arg Ile Phe
    210                 215                 220
Asp Asn Ala Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu Val Asp Glu
225                 230                 235                 240
Ile Ser Asn Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala Ala Asp Asn
                245                 250                 255
Phe Asp His Phe Arg Asn Ile Trp Lys Ser Ile Val Leu Lys Asp Met
            260                 265                 270
Phe Ile Tyr Cys Asp Leu Leu Leu Gln His Leu Ile Tyr Lys Phe Tyr
        275                 280                 285
Tyr Asp Asn Thr Val Asn Asp Ile Lys Lys Asn Phe Asp Glu Ser Trp
    290                 295                 300
Thr Gln Thr Leu Lys Glu
305                 310
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<210> 20
<211> 367
<212> PRT
<213> Babesia microti

<400> 20

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Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
 1                   5                  10                  15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp
            20                  25                  30
Pro Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val
        35                  40                  45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly
    50                  55                  60
Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
65                  70                  75                  80
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
                85                  90                  95
Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser Ser Glu
            100                 105                 110
Arg Phe Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg Ile Val Ile Phe
        115                 120                 125
Asn Glu Val Cys Leu Ser Tyr Ile Tyr Lys His Ser Val Met Ile Leu
    130                 135                 140
Glu Arg Asp Arg Val Asn Asp Gly His Lys Asp Tyr Ile Glu Glu Lys
145                 150                 155                 160
Thr Lys Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu Lys Cys Phe Pro
```

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                165                 170                 175
Glu Gln Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala Arg Ile Phe Asp
            180                 185                 190
Asn Ala Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu Val Asp Glu Ile
        195                 200                 205
Ser Asn Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala Ala Asp Asn Phe
    210                 215                 220
Asp His Phe Arg Asn Ile Trp Lys Ser Ile Val Leu Lys Asp Met Phe
225                 230                 235                 240
Ile Tyr Cys Asp Leu Leu Leu Gln His Leu Ile Tyr Lys Phe Tyr Tyr
                245                 250                 255
Asp Asn Thr Val Asn Asp Ile Lys Lys Asn Phe Asp Glu Ser Lys Ser
            260                 265                 270
Lys Ala Leu Val Leu Arg Asp Lys Ile Thr Lys Lys Asp Gly Asp Tyr
        275                 280                 285
Asn Thr His Phe Glu Asp Met Ile Lys Glu Leu Asn Ser Ala Ala Glu
    290                 295                 300
Glu Phe Asn Lys Ile Val Asp Ile Met Ile Ser Asn Ile Gly Asp Tyr
305                 310                 315                 320
Asp Glu Tyr Asp Ser Ile Ala Ser Phe Lys Pro Phe Leu Ser Met Ile
                325                 330                 335
Thr Glu Ile Thr Lys Ile Thr Lys Val Ser Asn Val Ile Ile Pro Gly
            340                 345                 350
Ile Lys Ala Leu Thr Leu Thr Val Phe Leu Ile Phe Ile Thr Lys
        355                 360                 365

      <210> 21
      <211> 492
      <212> PRT
      <213> Babesia microti

      <400> 21
Met Tyr Lys Ile Lys Ile Ser Asp Tyr Ile Ile Glu Phe Asp Asp Asn
 1               5                  10                  15
Ala Lys Leu Pro Thr Asp Asn Val Ile Gly Ile Ser Ile Tyr Thr Cys
            20                  25                  30
Glu His Asn Asn Pro Val Leu Ile Glu Phe Tyr Val Ser Lys Lys Gly
        35                  40                  45
Ser Ile Cys Tyr Tyr Phe Tyr Ser Met Asn Asn Asp Thr Asn Lys Trp
    50                  55                  60
Asn Asn His Lys Ile Lys Tyr Asp Lys Arg Phe Asn Glu His Thr Asp
65                  70                  75                  80
Met Asn Gly Ile His Tyr Tyr Tyr Ile Asp Gly Ser Leu Leu Ala Ser
                85                  90                  95
Gly Glu Val Thr Ser Asn Phe Arg Tyr Ile Ser Lys Glu Tyr Glu Tyr
            100                 105                 110
Glu His Thr Glu Leu Ala Lys Glu His Cys Lys Lys Glu Lys Cys Val
        115                 120                 125
Asn Val Asp Asn Ile Glu Asp Asn Asn Leu Lys Ile Tyr Ala Lys Gln
    130                 135                 140
Phe Lys Ser Val Val Thr Thr Pro Ala Asp Val Ala Gly Val Ser Asp
145                 150                 155                 160
Gly Phe Phe Ile Arg Gly Gln Asn Leu Gly Ala Val Gly Ser Val Asn
                165                 170                 175
Glu Gln Pro Asn Thr Val Gly Met Ser Leu Glu Gln Phe Ile Lys Asn
```

```
            180                 185                 190
Glu Leu Tyr Ser Phe Ser Asn Glu Ile Tyr His Thr Ile Ser Ser Gln
        195                 200                 205
Ile Ser Asn Ser Phe Leu Ile Met Met Ser Asp Ala Ile Val Lys His
    210                 215                 220
Asp Asn Tyr Ile Leu Lys Lys Glu Gly Glu Gly Cys Glu Gln Ile Tyr
225                 230                 235                 240
Asn Tyr Glu Glu Phe Ile Glu Lys Leu Arg Gly Ala Arg Ser Glu Gly
                245                 250                 255
Asn Asn Met Phe Gln Glu Ala Leu Ile Arg Phe Arg Asn Ala Ser Ser
            260                 265                 270
Glu Glu Met Val Asn Ala Ala Ser Tyr Leu Ser Ala Ala Leu Phe Arg
        275                 280                 285
Tyr Lys Glu Phe Asp Asp Glu Leu Phe Lys Lys Ala Asn Asp Asn Phe
    290                 295                 300
Gly Arg Asp Asp Gly Tyr Asp Phe Asp Tyr Ile Asn Thr Lys Lys Glu
305                 310                 315                 320
Leu Val Ile Leu Ala Ser Val Leu Asp Gly Leu Asp Leu Ile Met Glu
                325                 330                 335
Arg Leu Ile Glu Asn Phe Ser Asp Val Asn Asn Thr Asp Asp Ile Lys
            340                 345                 350
Lys Ala Phe Asp Glu Cys Lys Ser Asn Ala Ile Ile Leu Lys Lys Lys
        355                 360                 365
Ile Leu Asp Asn Asp Glu Asp Tyr Lys Ile Asn Phe Arg Glu Met Val
    370                 375                 380
Asn Glu Val Thr Cys Ala Asn Thr Lys Phe Glu Ala Leu Asn Asp Leu
385                 390                 395                 400
Ile Ile Ser Asp Cys Glu Lys Lys Gly Ile Lys Ile Asn Arg Asp Val
                405                 410                 415
Ile Ser Ser Tyr Lys Leu Leu Leu Ser Thr Ile Thr Tyr Ile Val Gly
            420                 425                 430
Ala Gly Val Glu Ala Val Thr Val Ser Val Ser Ala Thr Ser Asn Gly
        435                 440                 445
Thr Glu Ser Gly Gly Ala Gly Ser Gly Thr Gly Thr Ser Val Ser Ala
    450                 455                 460
Thr Ser Thr Leu Thr Gly Asn Gly Gly Thr Glu Ser Gly Gly Thr Ala
465                 470                 475                 480
Gly Thr Thr Thr Ser Ser Gly Thr Trp Phe Gly Lys
                485                 490
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<210> 22
<211> 138
<212> PRT
<213> Babesia microti

<400> 22

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Ser Leu Gly Gln Pro Ala Ser Leu Gly Gln Pro Ala Ser Leu Gly Gln
 1               5                  10                  15
Pro Ala Ser Leu Gly Gln Pro Ala Ser Leu Gly Gln Pro Ala Ser Leu
            20                  25                  30
Gly Gln Pro Val Pro Leu Gly Pro Pro Ala Ser Leu Gly Pro Pro Ala
        35                  40                  45
Ser Leu Gly Pro Pro Ala Ser Leu Gly Gln Pro Val Pro Leu Gly Pro
    50                  55                  60
Pro Ala Ser Leu Gly Pro Pro Ala Ser Leu Gly Pro Pro Ala Ser Leu
```

65 70 75 80
Gly Pro Pro Ala Ser Leu Gly Pro Pro Ala Ser Leu Gly Pro Pro Ala
85 90 95
Ser Leu Gly Pro Pro Ala Ser Leu Gly Pro Pro Ala Ser Leu Gly Pro
100 105 110
Thr Val Pro Leu Gly Pro Pro Ala Ser Arg Ser Val Ser Pro Ala Lys
115 120 125
Thr Ala Pro Leu Ile Lys Lys Ser Val Ile
130 135

<210> 23
<211> 303
<212> PRT
<213> Babesia microti

<400> 23
Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
1 5 10 15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Gly Asp Thr Asp
20 25 30
Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly
35 40 45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
50 55 60
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
65 70 75 80
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
85 90 95
Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu
100 105 110
Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro
115 120 125
Ser Glu Arg Phe Gly Tyr Gln Leu Leu Trp Tyr Ser Arg Arg Ile Val
130 135 140
Ile Phe Asn Glu Ile Tyr Leu Ser His Ile Tyr Glu His Ser Val Met
145 150 155 160
Ile Leu Glu Arg Asp Arg Val Asn Asp Gly His Lys Asp Tyr Ile Glu
165 170 175
Glu Lys Thr Lys Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu Lys Cys
180 185 190
Phe Pro Glu Gln Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala Arg Ile
195 200 205
Ile Asp Asn Ala Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu Val Asp
210 215 220
Glu Ile Ser Asn Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala Ala Asp
225 230 235 240
Asp Phe Asp His Phe Arg Asn Ile Trp Lys Ser Ile Val Pro Lys Asn
245 250 255
Met Phe Leu Tyr Cys Asp Leu Leu Leu Lys His Leu Ile Arg Lys Phe
260 265 270
Tyr Cys Asp Asn Thr Ile Asn Asp Ile Lys Lys Asn Phe Asp Asp Ile
275 280 285
Glu Lys Leu Gly Cys Phe Gln Ala Arg Ser Phe Leu Pro Val Asn
290 295 300

<210> 24
<211> 592
<212> PRT
<213> Babesia microti

<400> 24

```
Met Met Lys Phe Asn Ile Asp Lys Ile Ile Leu Ile Asn Leu Ile Val
 1               5                  10                  15
Leu Leu Asn Arg Asn Val Val Tyr Cys Val Asp Thr Asn Asn Ser Ser
            20                  25                  30
Leu Ile Glu Ser Gln Pro Val Thr Thr Asn Ile Asp Thr Asp Asn Thr
        35                  40                  45
Ile Thr Thr Asn Lys Tyr Thr Gly Thr Ile Ile Asn Ala Asn Ile Val
    50                  55                  60
Glu Tyr Arg Glu Phe Glu Asp Glu Pro Leu Thr Ile Gly Phe Arg Tyr
65                  70                  75                  80
Thr Ile Asp Lys Ser Gln Gln Asn Lys Leu Ser His Pro Asn Lys Ile
                85                  90                  95
Asp Lys Ile Lys Phe Ser Asp Tyr Ile Ile Glu Phe Asp Asp Asn Ala
            100                 105                 110
Lys Leu Pro Thr Asp Asn Val Ile Cys Ile Ser Ile Tyr Thr Cys Lys
        115                 120                 125
His Asn Asn Pro Val Leu Ile Arg Phe Ser Cys Ser Ile Glu Lys Tyr
    130                 135                 140
Tyr Tyr His Tyr Phe Tyr Ser Met Asn Asn Asp Thr Asn Lys Trp Asn
145                 150                 155                 160
Asn His Lys Leu Lys Tyr Asp Lys Thr Tyr Asn Glu Tyr Thr Asp Asn
                165                 170                 175
Asn Gly Val Asn Tyr Tyr Lys Ile Tyr Tyr Ser Asp Lys Gln Asn Ser
            180                 185                 190
Pro Thr Asn Gly Asn Glu Tyr Glu Asp Val Ala Leu Ala Arg Ile His
        195                 200                 205
Cys Asn Glu Glu Arg Cys Ala Asn Val Lys Val Asp Lys Ile Lys Tyr
    210                 215                 220
Lys Asn Leu Glu Ile Tyr Val Lys Gln Leu Gly Thr Ile Ile Asn Ala
225                 230                 235                 240
Asn Ile Val Glu Tyr Leu Val Phe Glu Asp Glu Pro Leu Thr Ile Gly
                245                 250                 255
Phe Arg Tyr Thr Ile Asp Lys Ser Gln Gln Asn Glu Leu Ser His Pro
            260                 265                 270
Asn Lys Ile Tyr Lys Ile Lys Phe Ser Asp Tyr Ile Ile Glu Phe Asp
        275                 280                 285
Asp Asp Ala Lys Leu Thr Thr Ile Gly Thr Val Glu Asp Ile Thr Ile
    290                 295                 300
Tyr Thr Cys Lys His Asn Asn Pro Val Leu Ile Arg Phe Ser Cys Ser
305                 310                 315                 320
Ile Glu Lys Tyr Tyr Tyr Tyr Tyr Phe Tyr Ser Met Asn Asn Asn Thr
                325                 330                 335
Asn Lys Trp Asn Asn His Asn Leu Lys Tyr Asp Asn Arg Phe Lys Glu
            340                 345                 350
His Ser Asp Lys Asn Gly Ile Asn Tyr Tyr Glu Ile Ser Ala Phe Lys
        355                 360                 365
Trp Ser Phe Ser Cys Phe Phe Val Asn Lys Tyr Glu His Lys Glu Leu
    370                 375                 380
Ala Arg Ile His Cys Asn Glu Glu Arg Cys Ala Asn Val Lys Val Asp
```

385 390 395 400
Lys Ile Lys Tyr Lys Asn Leu Glu Ile Tyr Val Lys Gln Leu Gly Thr
405 410 415
Ile Ile Asn Ala Asn Ile Val Glu Tyr Leu Val Phe Glu Asp Glu Pro
420 425 430
Leu Thr Ile Gly Phe Arg Tyr Thr Ile Asp Lys Ser Gln Gln Asn Glu
435 440 445
Leu Ser His Pro Asn Lys Ile Tyr Lys Ile Lys Phe Ser Asp Tyr Ile
450 455 460
Ile Glu Phe Asp Asp Asp Ala Lys Leu Thr Thr Ile Gly Thr Val Glu
465 470 475 480
Asp Ile Thr Ile Tyr Thr Cys Lys His Asn Asn Pro Val Leu Ile Arg
485 490 495
Phe Ser Cys Ser Ile Glu Lys Tyr Tyr Tyr Tyr Tyr Phe Tyr Ser Met
500 505 510
Asn Asn Asn Thr Asn Lys Trp Asn Asn His Asn Leu Lys Tyr Asp Asn
515 520 525
Arg Phe Lys Glu His Ser Asp Lys Asn Gly Ile Asn Tyr Tyr Glu Ile
530 535 540
Ser Ala Phe Lys Trp Ser Phe Ser Cys Phe Phe Val Asn Lys Tyr Glu
545 550 555 560
His Lys Glu Leu Ala Arg Ile His Cys Asn Glu Glu Lys Cys Val Asn
565 570 575
Val Lys Val Asp Asn Ile Gly Asn Lys Asn Leu Glu Ile Tyr Val Lys
580 585 590

<210> 25
<211> 463
<212> PRT
<213> Babesia microti

<400> 25
Ile Ile Met Lys Ile Asn Ile Asp Asn Ile Ile Leu Ile Asn Leu Ile
1 5 10 15
Ile Leu Leu Asn Arg Asn Val Val Tyr Cys Val Asp Lys Asn Asp Val
20 25 30
Ser Leu Trp Lys Ser Lys Pro Ile Thr Thr Val Ser Thr Thr Asn Asp
35 40 45
Thr Ile Thr Asn Lys Tyr Thr Ser Thr Val Ile Asn Ala Asn Phe Ala
50 55 60
Ser Tyr Arg Glu Phe Glu Asp Arg Glu Pro Leu Thr Ile Gly Phe Glu
65 70 75 80
Tyr Met Ile Asp Lys Ser Gln Gln Asp Lys Leu Ser His Pro Asn Lys
85 90 95
Ile Asp Lys Ile Lys Ile Ser Asp Tyr Ile Ile Glu Phe Asp Asp Asn
100 105 110
Ala Lys Leu Pro Thr Gly Ser Val Asn Asp Ile Ser Ile Ile Thr Cys
115 120 125
Lys His Asn Asn Pro Val Leu Ile Arg Phe Ser Cys Leu Ile Glu Gly
130 135 140
Ser Ile Cys Tyr Tyr Phe Tyr Leu Leu Asn Asn Asp Thr Asn Lys Trp
145 150 155 160
Asn Asn His Lys Leu Lys Tyr Asp Lys Thr Tyr Asn Glu His Thr Asp
165 170 175
Asn Asn Gly Ile Asn Tyr Tyr Lys Ile Asp Tyr Ser Glu Ser Thr Glu

```
            180                 185                 190
Pro Thr Thr Glu Ser Thr Thr Cys Phe Cys Phe Arg Lys Lys Asn His
        195                 200                 205
Lys Ser Glu Arg Lys Glu Leu Glu Asn Tyr Lys Tyr Glu Gly Thr Glu
    210                 215                 220
Leu Ala Arg Ile His Cys Asn Lys Gly Lys Cys Val Lys Leu Gly Asp
225                 230                 235                 240
Ile Lys Ile Lys Asp Lys Asn Leu Glu Ile Tyr Val Lys Gln Leu Met
                245                 250                 255
Ser Val Asn Thr Pro Val Asn Phe Asp Asn Pro Thr Ser Ile Asn Leu
            260                 265                 270
Pro Thr Val Ser Thr Thr Asn Asp Thr Ile Thr Asn Lys Tyr Thr Gly
        275                 280                 285
Thr Ile Ile Asn Ala Asn Ile Val Glu Tyr Cys Glu Phe Glu Asp Glu
    290                 295                 300
Pro Leu Thr Ile Gly Phe Arg Tyr Thr Ile Asp Lys Ser Gln Gln Asn
305                 310                 315                 320
Lys Leu Ser His Pro Asn Lys Ile Asp Lys Ile Lys Phe Phe Asp Tyr
                325                 330                 335
Ile Ile Glu Phe Asp Asp Asp Val Lys Leu Pro Thr Ile Gly Thr Val
            340                 345                 350
Asn Ile Ile Tyr Ile Tyr Thr Cys Glu His Asn Asn Pro Val Leu Val
        355                 360                 365
Glu Phe Ile Val Ser Ile Glu Glu Ser Tyr Tyr Phe Tyr Phe Tyr Ser
    370                 375                 380
Met Asn Asn Asn Thr Asn Lys Trp Asn Asn His Lys Leu Lys Tyr Asp
385                 390                 395                 400
Lys Arg Phe Lys Lys Tyr Thr Lys Asn Gly Ile Asn Cys Tyr Glu Tyr
                405                 410                 415
Val Leu Arg Lys Cys Ser Ser Tyr Thr Arg Lys Asn Glu Tyr Glu His
            420                 425                 430
Lys Glu Leu Ala Arg Ile His Cys Asn Glu Glu Lys Cys Val Asn Val
        435                 440                 445
Lys Val Asp Asn Ile Glu Lys Lys Asn Leu Glu Ile Tyr Val Lys
    450                 455                 460

      <210> 26
      <211> 297
      <212> PRT
      <213> Babesia microti

      <400> 26
Arg Ala Ala Arg Ala Asp Tyr Tyr Lys Tyr Leu Val Asp Glu Tyr Ser
 1               5                  10                  15
Ser Pro Arg Glu Glu Arg Glu Leu Ala Arg Val His Cys Asn Glu Glu
            20                  25                  30
Lys Cys Val Lys Leu Asp Gly Ile Lys Phe Lys Asp Lys Asn Leu Glu
        35                  40                  45
Ile Tyr Val Lys Gln Leu Met Ser Val Asn Thr Pro Val Val Phe Asp
    50                  55                  60
Asn Asn Thr Leu Ile Asn Pro Thr Ser Ser Ser Gly Ala Thr Asp Asp
65                  70                  75                  80
Ile Thr Tyr Glu Leu Ser Val Glu Ser Gln Pro Val Pro Thr Asn Ile
                85                  90                  95
Asp Thr Gly Asn Asn Ile Thr Thr Asn Thr Ser Asn Asn Asn Leu Ile
```

```
            100                 105                 110
Lys Ala Lys Phe Leu Tyr Asn Phe Asn Leu Pro Gly Lys Pro Ser Thr
        115                 120                 125
Gly Leu Phe Glu Tyr Thr Ile Asp Lys Ser Glu Gln Asn Lys Leu Ser
    130                 135                 140
His Pro Asn Lys Ile Asp Lys Ile Lys Phe Ser Asp Tyr Ile Ile Glu
145                 150                 155                 160
Phe Asp Asp Asp Ala Lys Leu Pro Thr Ile Gly Thr Val Asn Ile Ile
                165                 170                 175
Ser Ile Ile Thr Cys Lys His Asn Asn Pro Val Leu Val Glu Phe Ile
            180                 185                 190
Val Ser Thr Glu Ile Tyr Cys Tyr Tyr Asn Tyr Phe Tyr Ser Met Asn
        195                 200                 205
Asn Asn Thr Asn Lys Trp Asn Asn His Lys Leu Lys Tyr Asp Lys Arg
    210                 215                 220
Tyr Lys Glu Glu Tyr Thr Asp Asp Asn Gly Ile Asn Tyr Tyr Lys Leu
225                 230                 235                 240
Asn Asp Ser Glu Pro Thr Glu Ser Thr Glu Ser Thr Thr Cys Phe Cys
                245                 250                 255
Phe Arg Lys Lys Asn His Lys Tyr Glu Asn Glu Arg Thr Ala Leu Ala
            260                 265                 270
Lys Glu His Cys Asn Glu Glu Arg Cys Val Lys Val Asp Asn Ile Lys
        275                 280                 285
Asp Asn Asn Leu Glu Ile Tyr Leu Lys
    290                 295
```

<210> 27
<211> 121
<212> PRT
<213> Babesia microti

<400> 27

```
Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
 1                5                  10                  15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp
            20                  25                  30
Pro Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly
        35                  40                  45
Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
    50                  55                  60
Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro
65                  70                  75                  80
Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly
                85                  90                  95
Trp Ser Ser Glu Arg Phe Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg
            100                 105                 110
Ile Val Thr Phe Asn Glu Val Cys Leu
        115                 120
```

<210> 28
<211> 267
<212> PRT
<213> Babesia microti

<400> 28

```
Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
 1               5                  10                  15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp
            20                  25                  30
Pro Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly
        35                  40                  45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu
    50                  55                  60
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro
65                  70                  75                  80
Ser Glu Ala Gly Trp Ser Ser Glu Arg Phe Gly Tyr Gln Leu Leu Pro
                85                  90                  95
Tyr Ser Arg Arg Ile Val Thr Phe Asn Glu Val Cys Leu Ser Tyr Ile
            100                 105                 110
Tyr Lys His Ser Val Met Ile Leu Glu Arg Asp Arg Val Asn Asp Gly
        115                 120                 125
His Lys Asp Tyr Ile Glu Glu Lys Thr Lys Glu Lys Asn Lys Leu Lys
    130                 135                 140
Lys Glu Leu Glu Lys Cys Phe Pro Glu Gln Tyr Ser Leu Met Lys Lys
145                 150                 155                 160
Glu Glu Leu Ala Arg Ile Phe Asp Asn Ala Ser Thr Ile Ser Ser Lys
                165                 170                 175
Tyr Lys Leu Leu Val Asp Glu Ile Ser Asn Lys Ala Tyr Gly Thr Leu
            180                 185                 190
Glu Gly Pro Ala Ala Asp Asn Phe Asp His Phe Arg Asn Ile Trp Lys
        195                 200                 205
Ser Ile Val Leu Lys Asp Met Phe Ile Tyr Cys Asp Leu Leu Leu Gln
    210                 215                 220
His Leu Ile Tyr Lys Phe Tyr Tyr Asp Asn Thr Ile Asn Asp Ile Lys
225                 230                 235                 240
Lys Asn Phe Asp Glu Ser Lys Ser Lys Ala Leu Val Leu Arg Asp Lys
                245                 250                 255
Ile Thr Lys Lys Asp Val Tyr Val Asn Asp His
            260                 265
```

<210> 29
<211> 16
<212> PRT
<213> Babesia microti

<400> 29
```
Ala Trp Thr Phe Ser Val Leu Glu Leu Gln Glu Phe Ser Tyr Thr Val
 1               5                  10                  15
```

<210> 30
<211> 465
<212> PRT
<213> Babesia microti

<400> 30
```
Met Leu Thr Phe Gly Asn Ile Arg Phe His Asn Ile Asn Leu Pro Pro
 1               5                  10                  15
Phe Ser Leu Gly Ile Ile His Ser Ile Thr Val Glu Lys Ala Ile Asn
            20                  25                  30
Ser Glu Asp Phe Asp Gly Ile Gln Thr Leu Leu Gln Val Ser Ile Ile
```

```
          35                  40                  45
Ala Ser Tyr Gly Pro Ser Gly Asp Tyr Ser Ser Phe Val Phe Thr Pro
      50                  55                  60
Val Val Thr Ala Asp Thr Asn Val Phe Tyr Lys Leu Glu Thr Asp Phe
65                  70                  75                  80
Lys Leu Asp Val Asp Val Ile Thr Lys Thr Ser Leu Glu Leu Pro Thr
                85                  90                  95
Ser Val Pro Gly Phe His Tyr Thr Glu Thr Ile Tyr Gln Gly Thr Glu
            100                 105                 110
Leu Ser Lys Phe Ser Lys Pro Gln Cys Lys Leu Asn Asp Pro Pro Ile
        115                 120                 125
Thr Thr Gly Ser Gly Leu Gln Ile Ile His Asp Gly Leu Asn Asn Ser
    130                 135                 140
Thr Ile Ile Thr Asn Lys Glu Val Asn Val Asp Gly Thr Asp Leu Val
145                 150                 155                 160
Phe Phe Glu Leu Leu Pro Pro Ser Asp Gly Ile Pro Thr Leu Arg Ser
                165                 170                 175
Lys Leu Phe Pro Val Leu Lys Ser Ile Pro Met Ile Ser Thr Gly Val
            180                 185                 190
Asn Glu Leu Leu Leu Glu Val Leu Glu Asn Pro Ser Phe Pro Ser Ala
        195                 200                 205
Ile Ser Asn Tyr Thr Gly Leu Thr Gly Arg Leu Asn Lys Leu Leu Thr
    210                 215                 220
Val Leu Asp Gly Ile Val Asp Ser Ala Ile Ser Val Lys Thr Thr Glu
225                 230                 235                 240
Thr Val Pro Asp Asp Ala Glu Thr Ser Ile Ser Ser Leu Lys Ser Leu
                245                 250                 255
Ile Lys Ala Ile Arg Asp Asn Ile Thr Thr Thr Arg Asn Glu Val Thr
            260                 265                 270
Lys Asp Asp Val Tyr Ala Leu Lys Lys Ala Leu Thr Cys Leu Thr Thr
        275                 280                 285
His Leu Ile Tyr His Ser Lys Val Asp Gly Ile Ser Phe Asp Met Leu
    290                 295                 300
Gly Thr Gln Lys Asn Lys Ser Ser Pro Leu Gly Lys Ile Gly Thr Ser
305                 310                 315                 320
Met Asp Asp Ile Ile Ala Met Phe Ser Asn Pro Asn Met Tyr Leu Val
                325                 330                 335
Lys Val Ala Tyr Leu Gln Ala Ile Glu His Ile Phe Leu Ile Ser Thr
            340                 345                 350
Lys Tyr Asn Asp Ile Phe Asp Tyr Thr Ile Asp Phe Ser Lys Arg Glu
        355                 360                 365
Ala Thr Asp Ser Gly Ser Phe Thr Asp Ile Leu Leu Gly Asn Lys Val
    370                 375                 380
Lys Glu Ser Leu Ser Phe Ile Glu Gly Leu Ile Ser Asp Ile Lys Ser
385                 390                 395                 400
His Ser Leu Lys Ala Gly Val Thr Gly Gly Ile Ser Ser Ser Ser Leu
                405                 410                 415
Phe Asp Glu Ile Phe Asp Glu Leu Asn Leu Asp Gln Ala Thr Ile Arg
            420                 425                 430
Thr Leu Val Ala Pro Leu Asp Trp Pro Leu Ile Ser Asp Lys Ser Leu
        435                 440                 445
His Pro Ser Leu Lys Met Val Val Val Leu Pro Gly Phe Phe Ile Val
    450                 455                 460
Pro
465
```

<210> 31
<211> 128
<212> PRT
<213> Babesia microti

<400> 31
Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
1 5 10 15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp
20 25 30
Pro Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val
35 40 45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly
50 55 60
Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
65 70 75 80
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
85 90 95
Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser Ser Glu
100 105 110
Arg Phe Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg Ile Val Ile Phe
115 120 125

<210> 32
<211> 245
<212> PRT
<213> Babesia microti

<400> 32
Gln Glu Cys Cys Leu Val Val Lys Asp Lys Val Ile Arg His Ala Ala
1 5 10 15
Phe Ala Ala Thr Ile Ile Ile Arg Arg Arg Arg Val Ser Phe Ile Ile
20 25 30
Leu Gly Leu Ile Ile Ala Thr Met Thr Pro Phe Phe Thr Lys Val Phe
35 40 45
Phe Phe Gln Arg Cys Leu Ser Ile Met Arg Phe Tyr Ser Ser Leu Pro
50 55 60
Thr Phe Ile Leu Ile Glu Ile Ala Met Leu Phe Phe Met Ser Val Thr
65 70 75 80
Cys Phe Leu Arg Cys Leu Ser Ile Ile Arg Phe Tyr Ser Ser Ile Ser
85 90 95
Thr Phe Ile Leu Ile Asp Phe Val Met Pro Phe Phe Thr Leu Phe Thr
100 105 110
Tyr Phe Leu Arg Cys Leu Ser Ile Met Arg Phe Ser Phe Ser Leu Leu
115 120 125
Thr Phe Ile Arg Ile Asp Phe Val Met Pro Phe Phe Met Ser Val Thr
130 135 140
Cys Phe Leu Arg Cys Leu Ser Ile Ile Arg Phe Tyr Ser Ser Ile Ser
145 150 155 160
Thr Phe Ile Leu Ile Asp Phe Val Met Pro Phe Phe Thr Leu Phe Thr
165 170 175
Tyr Phe Leu Arg Cys Leu Ser Ile Ile Arg Phe Tyr Ser Ser Ile Ser
180 185 190
Thr Phe Ile Leu Ile Asp Phe Val Met Pro Phe Phe Thr Leu Phe Thr

```
        195                 200                 205
Tyr Phe Leu Arg Cys Leu Ser Ile Met Arg Phe Ser Phe Ser Leu Leu
    210                 215                 220
Thr Phe Ile Arg Ile Gly Phe Ala Met Pro Phe Phe Thr Leu Phe Ile
225                 230                 235                 240
Tyr Phe Leu Cys Arg
                245
```

<210> 33
<211> 293
<212> PRT
<213> Babesia microti

<400> 33

```
Thr Ala Phe Ala Ala Phe Leu Ala Phe Gly Asn Ile Ser Pro Val Leu
 1               5                  10                  15
Ser Ala Gly Gly Ser Gly Gly Asn Gly Gly Asn Gly Gly Gly His Gln
            20                  25                  30
Glu Gln Asn Asn Ala Asn Asp Ser Ser Asn Pro Thr Gly Ala Gly Gly
        35                  40                  45
Gln Pro Asn Asn Glu Ser Lys Lys Lys Ala Val Lys Leu Asp Leu Asp
    50                  55                  60
Leu Met Lys Glu Thr Lys Asn Val Cys Thr Thr Val Asn Thr Lys Leu
65                  70                  75                  80
Val Gly Lys Ala Lys Ser Lys Leu Asn Lys Leu Glu Gly Glu Ser His
                85                  90                  95
Lys Glu Tyr Val Ala Glu Lys Thr Lys Glu Ile Asp Glu Lys Asn Lys
            100                 105                 110
Lys Phe Asn Glu Asn Leu Val Lys Ile Glu Lys Lys Lys Lys Ile Lys
        115                 120                 125
Val Pro Ala Asp Thr Gly Ala Glu Val Asp Ala Val Asp Asp Gly Val
    130                 135                 140
Ala Gly Ala Leu Ser Asp Leu Ser Ser Asp Ile Ser Ala Ile Lys Thr
145                 150                 155                 160
Leu Thr Asp Asp Val Ser Glu Lys Val Ser Glu Asn Leu Lys Asp Asp
                165                 170                 175
Glu Ala Ser Ala Thr Glu His Thr Asp Ile Lys Glu Lys Ala Thr Leu
            180                 185                 190
Leu Gln Glu Ser Cys Asn Gly Ile Gly Thr Ile Leu Asp Lys Leu Ala
        195                 200                 205
Glu Tyr Leu Asn Asn Asp Thr Thr Gln Asn Ile Lys Lys Glu Phe Asp
    210                 215                 220
Glu Arg Lys Lys Asn Leu Thr Ser Leu Lys Thr Lys Val Glu Asn Lys
225                 230                 235                 240
Asp Glu Asp Tyr Val Asp Val Thr Met Thr Ser Lys Thr Asp Leu Ile
                245                 250                 255
Ile His Cys Leu Thr Cys Thr Asn Asp Ala His Gly Leu Phe Asp Phe
            260                 265                 270
Glu Ser Lys Ser Leu Ile Lys Gln Thr Phe Lys Leu Arg Ser Lys Asp
        275                 280                 285
Glu Gly Glu Leu Cys
    290
```

<210> 34
<211> 431

<212> PRT
<213> Babesia microti

<400> 34

```
Gly Pro Lys Met Lys Val Asn Ser Ala Asn Leu Asp Phe Arg Trp Ala
 1               5                  10                  15
Met Tyr Met Leu Asn Ser Lys Ile His Leu Ile Glu Ser Ser Leu Ile
            20                  25                  30
Asp Asn Phe Thr Leu Asp Asn Pro Ser Ala Tyr Glu Ile Leu Arg Val
        35                  40                  45
Ser Tyr Asn Ser Asn Glu Phe Gln Val Gln Ser Pro Gln Asn Ile Asn
    50                  55                  60
Asn Glu Met Glu Ser Ser Thr Pro Glu Ser Asn Ile Ile Trp Val Val
65                  70                  75                  80
His Ser Asp Val Ile Met Lys Arg Phe Asn Cys Lys Asn Arg Lys Ser
                85                  90                  95
Leu Ser Thr His Ser Leu Thr Glu Asn Asp Ile Leu Lys Phe Gly Arg
            100                 105                 110
Ile Glu Leu Ser Val Lys Cys Ile Ile Met Gly Ala Gly Ile Thr Ala
        115                 120                 125
Ser Asp Leu Asn Leu Lys Gly Leu Gly Phe Ile Ser Pro Asp Lys Gln
    130                 135                 140
Ser Thr Asn Val Cys Asn Tyr Phe Glu Asp Met His Glu Ser Tyr His
145                 150                 155                 160
Ile Leu Asp Thr Gln Arg Ala Ser Asp Cys Val Ser Asp Asp Gly Ala
                165                 170                 175
Asp Ile Asp Ile Ser Asn Phe Asp Met Val Gln Asp Gly Asn Ile Asn
            180                 185                 190
Ser Val Asp Ala Asp Ser Glu Thr Cys Met Ala Asn Ser Gly Val Thr
        195                 200                 205
Val Asn Asn Thr Glu Asn Val Ser Asn Ser Glu Asn Phe Gly Lys Leu
    210                 215                 220
Lys Ser Leu Val Ser Thr Thr Thr Pro Leu Cys Arg Ile Cys Leu Cys
225                 230                 235                 240
Gly Glu Ser Asp Pro Gly Pro Leu Val Thr Pro Cys Asn Cys Lys Gly
                245                 250                 255
Ser Leu Asn Tyr Val His Leu Glu Cys Leu Arg Thr Trp Ile Lys Gly
            260                 265                 270
Arg Leu Ser Ile Val Lys Asp Asp Asp Ala Ser Phe Phe Trp Lys Glu
        275                 280                 285
Leu Ser Cys Glu Leu Cys Gly Lys Pro Tyr Pro Ser Val Leu Gln Val
    290                 295                 300
Asp Asp Thr Glu Thr Asn Leu Met Asp Ile Lys Lys Pro Asp Ala Pro
305                 310                 315                 320
Tyr Val Val Leu Glu Met Arg Ser Asn Ser Gly Asp Gly Cys Phe Val
                325                 330                 335
Val Ser Val Ala Lys Asn Lys Ala Ile Ile Gly Arg Gly His Glu Ser
            340                 345                 350
Asp Val Arg Leu Ser Asp Ile Ser Val Ser Arg Met His Ala Ser Leu
        355                 360                 365
Glu Leu Asp Gly Gly Lys Val Val Ile His Asp Gln Gln Ser Lys Phe
    370                 375                 380
Gly Thr Leu Val Arg Ala Lys Ala Pro Phe Ser Met Pro Ile Lys Gly
385                 390                 395                 400
Pro Ile Cys Leu Gln Val Ser Ile Phe Phe Leu Asn Leu Lys Ile Ser
```

```
                405                 410                 415
Thr His Ser Leu Thr Met Glu Arg Gly Met Glu His Val Leu Leu
            420                 425                 430

      <210> 35
      <211> 6
      <212> PRT
      <213> Babesia microti

      <220>
      <221> VARIANT
      <222> (1)...(1)
      <223> Xaa = Glutamic Acid or Glycine

      <221> VARIANT
      <222> (2)...(2)
      <223> Xaa = Alanine or Threonine

      <221> VARIANT
      <222> (3)...(3)
      <223> Xaa = Glycine or Valine

      <221> VARIANT
      <222> (4)...(4)
      <223> Xaa = Tryptophan or Glycine

      <221> VARIANT
      <222> (5)...(5)
      <223> Xaa = Proline or Serine

      <400> 35
Xaa Xaa Xaa Xaa Xaa Ser
 1               5

      <210> 36
      <211> 32
      <212> PRT
      <213> Babesia microti

      <220>
      <221> VARIANT
      <222> (6)...(6)
      <223> Xaa = Methionine or Isoleucine

      <221> VARIANT
      <222> (9)...(9)
      <223> Xaa = Tyrosine or Serine

      <221> VARIANT
      <222> (10)...(10)
      <223> Xaa = Serine or Phenylalanine

      <221> VARIANT
      <222> (12)...(12)
      <223> Xaa = Leucine or Isoleucine
```

<221> VARIANT
<222> (13)...(13)
<223> Xaa = Proline, Serine or Leucine

<221> VARIANT
<222> (17)...(17)
<223> Xaa = Leucine or Arginine

<221> VARIANT
<222> (19)...(19)
<223> Xaa = Glutamic Acid, Aspartic Acid or Glycine

<221> VARIANT
<222> (20)...(20)
<223> Xaa = Isoleucine or Phenylalanine

<221> VARIANT
<222> (21)...(21)
<223> Xaa = Alanine or Valine

<221> VARIANT
<222> (23)...(23)
<223> Xaa = Leucine or Proline

<221> VARIANT
<222> (26)...(26)
<223> Xaa = Methionine or Threonine

<221> VARIANT
<222> (27)...(27)
<223> Xaa = Serine or Leucine

<221> VARIANT
<222> (28)...(28)
<223> Xaa = Valine or Phenylalanine

<221> VARIANT
<222> (29)...(29)
<223> Xaa = Threonine or Isoleucine

<221> VARIANT
<222> (30)...(30)
<223> Xaa = Cysteine ro Tyrosine

<400> 36

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Arg Cys Leu Ser Ile Xaa Arg Phe Xaa Xaa Ser Xaa Xaa Thr Phe Ile
 1               5                  10                  15
Xaa Ile Xaa Xaa Xaa Met Xaa Phe Phe Xaa Xaa Xaa Xaa Xaa Phe Leu
            20                  25                  30
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<210> 37
<211> 1820
<212> DNA
<213> Babesia microti

<400> 37
cggcacgagt agcccccacc atcttttgca ttcatttcaa gtttctccaa atctcgatgg 60
gacctccaat tttggctcca ccacaaacaa gtctgacata ttgagcaaaa catattgatt 120
taatttaaag aacagacatc tggccattca tgctaagagg tctcttcatt gttgagtggg 180
aacagccttg tatacgggct tacaacacaa tggaaaaaca ccttgtagaa gagatcatgc 240
ttcactcagt gctagatgtt gatgccagtg atttgcttgg ggtagtaagc cagtactaga 300
atacaggatg cacttggact ggcaaacaga atacacctgt tgcctgaata gaaactcaca 360
gagacccgat gctgtctggt accaacaagg ttctgcttct gggaagaatt tacagatatt 420
atgttgggaa aagagacacc ctgtatgtgt agaaacaaag aagcacagat cttagatgaa 480
ttaatataag aatgatactt ctctagaaac aaatgtagtt accaactata ttccagaacc 540
caatgcggat tcagaatctg tacatgttga aatccaggaa catgataaca tcaatccaca 600
agacgcttgc gatagtgagc cgctcgaaca aatggattct gataccaggg tgttgcccga 660
aagtttggat gaggggtac cacaccaatt ctctagatta gggcaccact cagacatggc 720
atctgatata aatgatgaag aaccatcatt taaaatcggc gagaatgaca taattcaacc 780
accctgggaa gatacagctc cataccattc aatagatgat gaagagcttg acaacttaat 840
gagactaacg gcgcaagaaa caagtgacga tcatgaagaa gggaatggca aactcaatac 900
gaataaaagt gagaagactg aaagaaaatc gcatgatact cagacaccgc aagaaatata 960
tgaagagctt gacaacttac tgagactaac ggcacaagaa atatatgaag agcgtaaaga 1020
agggcatggc aaacccaata cgaataaaag tgagaaggct gaaagaaaat cgcatgatac 1080
tcagacaacg caagaaatat gtgaagagtg tgaagaaggg catgacaaaa tcaataagaa 1140
taaaagtgga aatgctggaa taaaatcgta tgatactcag acaacgcaag aaatatgtga 1200
agagtgtgaa gaagggcatg acaaaatcaa taagaataaa agtggaaatg ctggaataaa 1260
atcgtatgat actcagacac cgcaggaaac aagtgacgct catgaagaag ggcatgacaa 1320
aatcaatacg aataaaagtg agaaggctga aagaaaatcg catgatactc agacaacgca 1380
agaaatatgt gaagagtgtg aagaagggca tgacaaaatc aataagaata aaagtggaaa 1440
tgctggaata aaatcgtatg atactcagac accgcaggaa acaagtgacg ctcatgaaga 1500
agagcatggc aatctcaata agaataaaag tgggaaggct ggaataaaat cgcataatac 1560
tcagacaccg ctgaaaaaaa aagacttttg taaagaaggg tgtcatggtt gcaataataa 1620
gcccgaggat aatgaaagag acccgtcgtc gcctgatgat gatggtggct gcgaatgcgg 1680
catgacgaat cactttgtct ttgactacaa gacaacactc ttgttaaaga gcctcaagac 1740
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atgcatgttt aaggctttcc 1820

<210> 38
<211> 445
<212> PRT
<213> Babesia microti

<400> 38
Tyr Lys Asn Asp Thr Ser Leu Glu Thr Asn Val Val Thr Asn Tyr Ile
1 5 10 15
Pro Glu Pro Asn Ala Asp Ser Glu Ser Val His Val Glu Ile Gln Glu
20 25 30
His Asp Asn Ile Asn Pro Gln Asp Ala Cys Asp Ser Glu Pro Leu Glu
35 40 45
Gln Met Asp Ser Asp Thr Arg Val Leu Pro Glu Ser Leu Asp Glu Gly
50 55 60
Val Pro His Gln Phe Ser Arg Leu Gly His His Ser Asp Met Ala Ser
65 70 75 80
Asp Ile Asn Asp Glu Glu Pro Ser Phe Lys Ile Gly Glu Asn Asp Ile
85 90 95
Ile Gln Pro Pro Trp Glu Asp Thr Ala Pro Tyr His Ser Ile Asp Asp
100 105 110
Glu Glu Leu Asp Asn Leu Met Arg Leu Thr Ala Gln Glu Thr Ser Asp

```
        115                 120                 125
Asp His Glu Glu Gly Asn Gly Lys Leu Asn Thr Asn Lys Ser Glu Lys
    130                 135                 140
Thr Glu Arg Lys Ser His Asp Thr Gln Thr Pro Gln Glu Ile Tyr Glu
145                 150                 155                 160
Glu Leu Asp Asn Leu Leu Arg Leu Thr Ala Gln Glu Ile Tyr Glu Glu
                165                 170                 175
Arg Lys Glu Gly His Gly Lys Pro Asn Thr Asn Lys Ser Glu Lys Ala
            180                 185                 190
Glu Arg Lys Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu
        195                 200                 205
Cys Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala
    210                 215                 220
Gly Ile Lys Ser Tyr Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu
225                 230                 235                 240
Cys Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala
                245                 250                 255
Gly Ile Lys Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala
            260                 265                 270
His Glu Glu Gly His Asp Lys Ile Asn Thr Asn Lys Ser Glu Lys Ala
        275                 280                 285
Glu Arg Lys Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu
    290                 295                 300
Cys Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala
305                 310                 315                 320
Gly Ile Lys Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala
                325                 330                 335
His Glu Glu Glu His Gly Asn Leu Asn Lys Asn Lys Ser Gly Lys Ala
            340                 345                 350
Gly Ile Lys Ser His Asn Thr Gln Thr Pro Leu Lys Lys Lys Asp Phe
        355                 360                 365
Cys Lys Glu Gly Cys His Gly Cys Asn Asn Lys Pro Glu Asp Asn Glu
    370                 375                 380
Arg Asp Pro Ser Ser Pro Asp Asp Asp Gly Gly Cys Glu Cys Gly Met
385                 390                 395                 400
Thr Asn His Phe Val Phe Asp Tyr Lys Thr Thr Leu Leu Leu Lys Ser
                405                 410                 415
Leu Lys Thr Glu Thr Ser Thr His Tyr Tyr Ile Ala Met Ala Ala Ile
            420                 425                 430
Phe Thr Ile Ser Leu Phe Pro Cys Met Phe Lys Ala Phe
        435                 440                 445
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<210> 39
<211> 32
<212> PRT
<213> Babesia microti

<220>
<221> VARIANT
<222> (3)...(3)
<223> Xaa = Glycine or Aspartic Acid

<221> VARIANT
<222> (5)...(5)
<223> Xaa = Proline or Isoleucine

<221> VARIANT
<222> (7)...(7)
<223> Xaa = Lysine or Threonine

<221> VARIANT
<222> (11)...(11)
<223> Xaa = Glutamic Acid or Glycine

<221> VARIANT
<222> (12)...(12)
<223> Xaa = Lysine or Asparagine

<221> VARIANT
<222> (14)...(14)
<223> Xaa = Glutamic Acid or Glycine

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Isoleucine or Arginine

<221> VARIANT
<222> (18)...(18)
<223> Xaa = Histidine or Tyrosine

<221> VARIANT
<222> (23)...(23)
<223> Xaa = Threonine or Proline

<221> VARIANT
<222> (26)...(26)
<223> Xaa = Isoleucine or Threonine

<221> VARIANT
<222> (27)...(27)
<223> Xaa = Cysteine or Serine

<221> VARIANT
<222> (28)...(28)
<223> Xaa = Aspartic Acid or Glutamic Acid

<221> VARIANT
<222> (29)...(29)
<223> Xaa = Glutamic Acid or Alanine

<221> VARIANT
<222> (30)...(30)
<223> Xaa = Cysteine or Histidine

<400> 39

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Gly His Xaa Lys Xaa Asn Xaa Asn Lys Ser Xaa Xaa Ala Xaa Xaa Lys
 1               5                  10                  15
Ser Xaa Asp Thr Gln Thr Xaa Gln Glu Xaa Xaa Xaa Xaa Xaa Glu Glu
            20                  25                  30
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<210> 40
<211> 2430
<212> DNA
<213> Babesia microti

<400> 40
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gtaccactaa tgatactatt acaaatacac acactactaa tgtaattaat gccaatctta 120
ttggccactt taattataag gatagggaac ctttaacaat agtatttgta tacatgatcg 180
atgaatcaga acaaaataaa ttatcacatc cgaataaaat tgataaaatc aaaatttctg 240
attatataat tgaatttgat gacaatgcta aattaccaac tggtagtgtt attgatttaa 300
acatctatac ttgcaaacat aataatccag tattaattga attttatgtt tctatagaag 360
gatctttctg ctattatttc tctcattgaa taatgataca aatgaatgga ataatcacaa 420
aataaaatat gataaaaaat ataaagaata tacggacatg aatggtattc attattatta 480
tattgatggt agtttacttg taagtggcga agttacatct aattttcgtt atatttctaa 540
agaatatgaa tatgagcata caggattagt aaaaaaatat tgtaatgaag aaagatgtgt 600
aaaattggat aacattaaga taaaggataa taatttggaa atttatgtga aataatttaa 660
tgaagtataa tattatttat aataattcaa agattaatat aatcaattat tataattaca 720
aaaataatta attgtagaat attatattat taatcaattc agattataaa tacatatttt 780
tacatacatt tcaatttaaa cattcaaatt aatgtcattt ttatctacat tattataatt 840
ataactataa tattcattaa atactattaa aaaaaatatc ctctacatta tattaattat 900
tatagtatgt cattatataa catattcaca acgtataaca aatcaatcat taacatatac 960
atatatgata tcattaataa tcaatattta attgatacaa taatcaatag tcatctgtaa 1020
tataatcatt gtatactaat ttattataaa ttattacaaa atacactctt ttacttcatt 1080
ttatttctgt taaatttcat attctaatat tatattcatc tttctcatgt tactttaatc 1140
tatttccata tttatcccaa tttcttcatt taagactgag atgttcgttc gttcatacat 1200
aaataatgtg taaattttgt aatatataat aatgtataca tctggtatta catctatttt 1260
gtaataaata ttaaaaaaac ggttaaagtt agtgccttaa ttccaggaat tattacatta 1320
gaaactttgg tgattttagt gatttcggtg atcattgaaa gaaatggttt gaaacttgca 1380
atactgtcat actcatcata atccccaatg ttggaaatca tgatgtcaac aattttatta 1440
aattcttctg ctgcactatt caactcctta atcatgtcct caaaatgagt gttataatct 1500
ccatcctttt tagtgatctt atccctcaaa actaaagctt tagatttgga ttcgtcaaaa 1560
tttttcttga tatcattaac ggtattgtca taatagaatt tatagattaa atgttgtaat 1620
aataagtcac aatatataaa catatcttta agtacaatag acttccatat attacggaaa 1680
tggtcaaaat tatcagcagc tggaccttcc aatgtaccat aggccttgtt tgatatttca 1740
tcaaccaata acttatattt tgaagagata gtggatgcat tatcaaatat tctagccaat 1800
tcttctttct tcataaggga atattgttca ggaaaacatt tttccaattc ttttttcaat 1860
ttattcttct ccttggtttt ttcttcaatg tagtctttat gaccatcgtt caccctatct 1920
cgttccaata tcataacact atgtttgtat atataagata aacaaacttc attaaatata 1980
actattcttc tagaatacgg aagaagctga tatccaaatc gttcactaga ccaaccagct 2040
tcactaggcc aaccagttcc actaggccaa ccagttccac taggcccacc agcttcacta 2100
ggcccaccag cttcactagg cccaccagct tcactaggcc caccagcttc actaggccaa 2160
ccagttccac taggcccacc agcttcacta ggcccaccag cttcactggg cccaacagtt 2220
ccactaggcc caccagcttc actaggccca ccagcttcgg gatcggtatc acttgcaaag 2280
acagcaccgc tcattaaaaa gagtgtaata taaggaacta atattgattt aaatgacacc 2340
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gtggtagtga ttgtggtgct gcatctagtt 2430

<210> 41
<211> 128
<212> PRT
<213> Babesia microti

<400> 41
Tyr Cys Val Asp Lys Asn Asp Val Ser Leu Trp Lys Ser Lys Pro Ile

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 1               5                  10                  15
Thr Thr Val Ser Thr Thr Asn Asp Thr Ile Thr Asn Thr His Thr Thr
            20                  25                  30
Asn Val Ile Asn Ala Asn Leu Ile Gly His Phe Asn Tyr Lys Asp Arg
        35                  40                  45
Glu Pro Leu Thr Ile Val Phe Val Tyr Met Ile Asp Glu Ser Glu Gln
    50                  55                  60
Asn Lys Leu Ser His Pro Asn Lys Ile Asp Lys Ile Lys Ile Ser Asp
65                  70                  75                  80
Tyr Ile Ile Glu Phe Asp Asp Asn Ala Lys Leu Pro Thr Gly Ser Val
                85                  90                  95
Ile Asp Leu Asn Ile Tyr Thr Cys Lys His Asn Asn Pro Val Leu Ile
            100                 105                 110
Glu Phe Tyr Val Ser Ile Glu Gly Ser Phe Cys Tyr Tyr Phe Ser His
        115                 120                 125
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<210> 42
<211> 1271
<212> DNA
<213> Babesia microti

<400> 42

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tgagaaaacg catataattg taactacgcc agagaagttt gacgtagtta cacgtaaaac     60
aggcaatgag cccctgcttg agcggcttag attggttata attgatgaaa tacacctact    120
ccatgacact aggggtccag tgctggaggc tattgtggcc cgcctgagtc agaggcccga    180
acgcgtaagg ctagttggtc tatcggccac gcttccaaac tacgaagacg tggctagatt    240
tctcactgtt aatctagacc gagggctttt ctactttggc agccacttta ggcctgtgcc    300
cttggagcag gtgtattatg gcgtgaagga gaagaaggct atcaaacgtt tcaacgcaat    360
caacgaaatt ctctaccaag aggtgattaa cgatgtttct agctgccaaa ttcttgtttt    420
tgtgcattct agaaaggaaa cgtacaggac ggcaaaattt atcaaagaca cggccctttc    480
acgggacaac ttgggagcct aaaccctaaa ccctaaaccc taaaccctaa ccctaaaccc    540
taaaccctaa accctaaacc ctaaacccta accctaaccc taaccctaac cctaacctag    600
ccttcattga cgtctatccc caatcttaga aaaatcttca aatcgattct agaataactg    660
gaagcaatta tcagaaattg tataactgct tattagctta ttagcttatt agttaggatg    720
tatgcacatt gatgacaact agatgcagca ccacaatcac taccacgtac caatcatata    780
ccaataatgt actaataatg taccaataac tatggtttat aaagatggtg tcatttaaat    840
caatattagt tccttatatt acactctttt taatgagcgg tgctgtcttt gcaggtgata    900
ccgatcgcga agctggtggg cctagtggaa ctgttgggcc tagtgaagct ggtgggccta    960
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ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg   1080
ggcctagtgg aactggttgg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta   1140
gtgaagctgg tgggcctagt ggaactggtt ggcctagtga agctggttgg cctagtgaag   1200
ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt   1260
ggcctagtga a                                                        1271
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<210> 43
<211> 166
<212> PRT
<213> Babesia microti

<400> 43

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Glu Lys Thr His Ile Ile Val Thr Thr Pro Glu Lys Phe Asp Val Val
 1               5                  10                  15
Thr Arg Lys Thr Gly Asn Glu Pro Leu Leu Glu Arg Leu Arg Leu Val
            20                  25                  30
```

```
Ile Ile Asp Glu Ile His Leu Leu His Asp Thr Arg Gly Pro Val Leu
        35                  40                  45
Glu Ala Ile Val Ala Arg Leu Ser Gln Arg Pro Glu Arg Val Arg Leu
    50                  55                  60
Val Gly Leu Ser Ala Thr Leu Pro Asn Tyr Glu Asp Val Ala Arg Phe
65                  70                  75                  80
Leu Thr Val Asn Leu Asp Arg Gly Leu Phe Tyr Phe Gly Ser His Phe
                85                  90                  95
Arg Pro Val Pro Leu Glu Gln Val Tyr Tyr Gly Val Lys Glu Lys Lys
            100                 105                 110
Ala Ile Lys Arg Phe Asn Ala Ile Asn Glu Ile Leu Tyr Gln Glu Val
        115                 120                 125
Ile Asn Asp Val Ser Ser Cys Gln Ile Leu Val Phe Val His Ser Arg
    130                 135                 140
Lys Glu Thr Tyr Arg Thr Ala Lys Phe Ile Lys Asp Thr Ala Leu Ser
145                 150                 155                 160
Arg Asp Asn Leu Gly Ala
                165
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<210> 44
<211> 154
<212> PRT
<213> Babesia microti

<400> 44

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Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
 1               5                  10                  15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Gly Asp Thr Asp
            20                  25                  30
Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly
        35                  40                  45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
    50                  55                  60
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
65                  70                  75                  80
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
                85                  90                  95
Trp Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
            100                 105                 110
Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Pro
        115                 120                 125
Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly
    130                 135                 140
Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu
145                 150
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<210> 45
<211> 4223
<212> DNA
<213> Babesia microti

<400> 45

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ctcgtgcctt tctcaactga taacagctaa caaaaagtct cttatcttaa accatcctat      60
acctcgtatt ataatatgaa aagggccttt tctaaatctt tccccaaagt tctgctattt     120
aattaaaaaa aaaaaagact cattcaataa acgggtgggg cagaaagggt acctttccaa     180
```

gtgttcttcc atgacgaccc acaatgcaaa gttcttctta caaagaaaag agaaagatcc 240
actgagtgat aagtaaccca gctggggccg ggcggtggtg gcgcacacct ttaatcccag 300
cactcgggag gcagaggcag gcggatctct gtgagttcga gaccaggctg gaccgacagc 360
ctccaaaaca atacagagaa accctgtctc ataaaaaacc aaaaaaaaag taacccagct 420
ggatttggta actgtctcag aaacagacta tataaaacct catcacccta caacaagtag 480
gaagctagcg ctccccaccc catcccaaca cacacacaca cacacacaca cacacacaca 540
cacacacaca cacgcacaca cgcacgcacg cacacacgca cgcacgcaca cacgcacaca 600
cgcacgcaca cacgcacaca cgcacgcacg cacgcacgca cgcacgcacg cacgcccttc 660
tgtgtctgtt ctgttcaaga agggtaccac aaaaaagtac cttatggcca catcaatgac 720
aattattact gtatataaaa tgccccccatg gatggcattg tattgtcgaa attaaaggca 780
cccccgaaag aacagcacag aggggctacc accaattaac tcccaggagg aaataaagac 840
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caaggagtaa cagggacaaa agcagcagat ggtgccaggc aggagtgtgc ctaccacacc 960
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taactgattt aaggaacaac tttctgctca ttgcctctat cttctcaaac atttcgaagc 1140
agttattttt tataagaaaa tataaaacag gccgactaaa ttcgatcttt ctctccccag 1200
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tcctactaca gacgttaggg aacatatgtg aaaacctggt gtacaaccta aatcataact 1620
agacagaaga cagcactatt tcctggtcac atagaaagca gaatagcatc ctcacaccaa 1680
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aaatgttaca gatcattgct ttttttcttt tttagaagac atcaaaacaa taggatttct 1920
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aacagactca agaaagtaag aacaggaatt tggagcttgc aacactgatg ttctttgtaa 2040
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accctaaacc ctaaacccta aaccctaaac cctaaaccct aaccctaacc ctaaccctaa 2640
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tagaataact ggaagcaatt atcagaaatt gtataactgc ttattagctt attagcttat 2760
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ccaatcatat accaataatg tactaataat gtaccaataa ctatggttta taaagatggt 2880
gtcatttaaa tcaatattag ttccttatat tacactcttt ttaatgagcg gtgctgtctt 2940
tgcaggtgat accgatcgcg aagctggtgg gcctagtgga actgttgggc ctagtgaagc 3000
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gcctagtgaa gctggtgggc ctagtgaagc tggtgggcct agtgaagctg gtgggcctag 3120
tggaactgtt gggcctagtg aagctggtgg gcctagtgaa gctggtgggc ctagtgaagc 3180
tggtgggcct agtgaagctg gttggcctag tgaagctggt tggcctagtg aagctggttg 3240
gcctagtgaa gctggttggc ctagtgaagc tggttggcct agtgaagctg gttggcctag 3300
tgaacgattt ggatatcagc ttctttggta ttctagaaga atagttatat ttaatgaaat 3360
ttatttatct catatatacg aacatagtgt tatgatattg gaacgagata gggtgaacga 3420
tggtcataaa gactacattg aagaaaaaac caaggagaag aataaattga aaaaagaatt 3480

ggaaaaatgt tttcctgaac aatattccct tatgaagaaa gaagaattgg ctagaataat 3540
tgataatgca tccactatct cttcaaaata taagttattg gttgatgaaa tatccaacaa 3600
agcctatggt acattggaag gtccagctgc tgatgatttt gaccatttcc gtaatatatg 3660
gaagtctatt gtacctaaaa atatgtttct atattgtgac ttattattaa aacatttaat 3720
ccgtttaacc cccagaaaga gctgaccaga caaaggttaa ctcttgaatc ccaggcatca 3780
gcctgggaat ccatcatggg actgatcaag acccctgaa tgtgggtgtc agtgaggagg 3840
cctaggtaat ctattgagcc tcgggcagca gatcagtacc catcccaatt atacacaatt 3900
gcagtgttgt ggtttcacag tgaataattg taggtcacag tccattatat tgatgtcaca 3960
gtttttaatt gtcatgtcac agtgcaagct agtgatgtca gagtgtataa ctgtgttcat 4020
agagaatgta ttgatgtcac agtcaataat cgtgatgtca tagtgcagta tattgatgtc 4080
acaatgtata attgtgatgt taaagtgcaa gatagtgaag tcacagtata taattgtgat 4140
gtcatattgc attataatga tgtcacactt tataatttct tacatacagc actatagtga 4200
tgtaacagcc aataattgtg atg 4223

<210> 46
<211> 294
<212> PRT
<213> Babesia microti

<400> 46

Leu Trp Phe Ile Lys Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr
1 5 10 15
Ile Thr Leu Phe Leu Met Ser Gly Ala Val Phe Ala Gly Asp Thr Asp
20 25 30
Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly
35 40 45
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
50 55 60
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
65 70 75 80
Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala Gly
85 90 95
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
100 105 110
Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro
115 120 125
Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly
130 135 140
Trp Pro Ser Glu Arg Phe Gly Tyr Gln Leu Leu Trp Tyr Ser Arg Arg
145 150 155 160
Ile Val Ile Phe Asn Glu Ile Tyr Leu Ser His Ile Tyr Glu His Ser
165 170 175
Val Met Ile Leu Glu Arg Asp Arg Val Asn Asp Gly His Lys Asp Tyr
180 185 190
Ile Glu Glu Lys Thr Lys Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu
195 200 205
Lys Cys Phe Pro Glu Gln Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala
210 215 220
Arg Ile Ile Asp Asn Ala Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu
225 230 235 240
Val Asp Glu Ile Ser Asn Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala
245 250 255
Ala Asp Asp Phe Asp His Phe Arg Asn Ile Trp Lys Ser Ile Val Pro
260 265 270
Lys Asn Asn Phe Leu Tyr Cys Asp Leu Leu Leu Lys His Leu Ile Arg

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       275                 280                 285
Leu Thr Pro Arg Lys Ser
    290

      <210> 47
      <211> 30
      <212> PRT
      <213> Artificial Sequence

      <220>
      <223> Synthetic peptide of repeat region of antigen
            BMNI-3 (SEQ ID NO:3)

      <400> 47
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly
 1               5                  10                  15
Trp Thr Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser
            20                  25                  30

      <210> 48
      <211> 30
      <212> PRT
      <213> Artificial Sequence

      <220>
      <223> Synthetic peptide of repeat region of antigen
            BMNI-3 (SEQ ID NO:3)

      <400> 48
Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Gly Thr Gly Trp
 1               5                  10                  15
Pro Ser Glu Ala Gly Trp Gly Ser Glu Ala Gly Trp Ser Ser
            20                  25                  30

      <210> 49
      <211> 367
      <212> PRT
      <213> Babesia microti

      <400> 49
Met Val Ser Phe Lys Ser Ile Leu Val Pro Tyr Ile Thr Leu Phe Leu
 1               5                  10                  15
Met Ser Gly Ala Val Phe Ala Ser Asp Thr Asp Pro Glu Ala Gly Gly
            20                  25                  30
Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro Ser Glu Ala
        35                  40                  45
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser
    50                  55                  60
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
65                  70                  75                  80
Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Ser Glu Ala Gly Gly
                85                  90                  95
Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Ser Ser Glu
            100                 105                 110
Arg Phe Gly Tyr Gln Leu Leu Pro Tyr Ser Arg Arg Ile Val Ile Phe
```

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        115                 120                 125
Asn Glu Val Cys Leu Ser Tyr Ile Tyr Lys His Ser Val Met Ile Leu
    130                 135                 140
Glu Arg Asp Arg Val Asn Asp Gly His Lys Asp Tyr Ile Glu Glu Lys
145                 150                 155                 160
Thr Lys Glu Lys Asn Lys Leu Lys Lys Glu Leu Glu Lys Cys Phe Pro
                165                 170                 175
Glu Gln Tyr Ser Leu Met Lys Lys Glu Glu Leu Ala Arg Ile Phe Asp
            180                 185                 190
Asn Ala Ser Thr Ile Ser Ser Lys Tyr Lys Leu Leu Val Asp Glu Ile
        195                 200                 205
Ser Asn Lys Ala Tyr Gly Thr Leu Glu Gly Pro Ala Ala Asp Asn Phe
    210                 215                 220
Asp His Phe Arg Asn Ile Trp Lys Ser Ile Val Leu Lys Asp Met Phe
225                 230                 235                 240
Ile Tyr Cys Asp Leu Leu Leu Gln His Leu Ile Tyr Lys Phe Tyr Tyr
                245                 250                 255
Asp Asn Thr Val Asn Asp Ile Lys Lys Asn Phe Asp Glu Ser Lys Ser
            260                 265                 270
Lys Ala Leu Val Leu Arg Asp Lys Ile Thr Lys Lys Asp Gly Asp Tyr
        275                 280                 285
Asn Thr His Phe Glu Asp Met Ile Lys Glu Leu Asn Ser Ala Ala Glu
    290                 295                 300
Glu Phe Asn Lys Ile Val Asp Ile Met Ile Ser Asn Ile Gly Asp Tyr
305                 310                 315                 320
Asp Glu Tyr Asp Ser Ile Ala Ser Phe Lys Pro Phe Leu Ser Met Ile
                325                 330                 335
Thr Glu Ile Thr Lys Ile Thr Lys Val Ser Asn Val Ile Ile Pro Gly
            340                 345                 350
Ile Lys Ala Leu Thr Leu Thr Val Phe Leu Ile Phe Ile Thr Lys
        355                 360                 365
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<210> 50
<211> 1908
<212> DNA
<213> Babesia microti

<400> 50

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aaaagattta atgaacatac tgacatgaat ggtattcatt attattatat tgatggtagt      60
ttacttgcga gtggcgaagt tacatctaat tttcgttata tttctaaaga atatgaatat     120
gagcatacag aattagcaaa agagcattgc aagaaagaaa aatgtgtaaa tgtggataac     180
attgaggata ataatttgaa aatatatgcg aaacagttta atctgtagt tactactcca      240
gctgatgtag cgggtgtgtc agatggattt tttatacgtg gccaaaatct tggtgctgtg     300
ggcagtgtaa atgaacaacc taatactgtt ggtatgagtt tagaacaatt catcaagaac     360
gagctttatt cttttagtaa tgaaatttat catacaatat ctagtcaaat cagtaattct     420
ttcttaataa tgatgtctga tgcaattgtt aaacatgata actatatttt aaaaaaagaa     480
ggtgaaggct gtgaacaaat ctacaattat gaggaattta tagaaaagtt gaggggtgct     540
agaagtgagg ggaataatat gtttcaggaa gctctgataa ggtttaggaa tgctagtagt     600
gaagaaatgg ttaatgctgc aagttatcta tccgccgccc ttttcagata taaggaattt     660
gatgatgaat tattcaaaaa ggccaacgat aattttggac gcgatgatgg atatgatttt     720
gattatataa atacaaagaa agagttagtt atacttgcca gtgtgttgga tggtttggat     780
ttaataatgg aacgtttgat cgaaaatttc agtgatgtca ataatacaga tgatattaag     840
aaggcatttg acgaatgcaa atctaatgct attatattga agaaaaagat acttgacaat     900
gatgaagatt ataagattaa ttttagggaa atggtgaatg aagtaacatg tgcaaacaca     960
aaatttgaag ccctaaatga tttgataatt tccgactgtg agaaaaaagg tattaagata    1020
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aacagagatg tgatttcaag ctacaaattg cttctttcca caatcaccta tattgttgga 1080
gctggagttg aagctgtaac tgttagtgtg tctgctacat ctaatggaac tgaatctggt 1140
ggagctggta gtggaactgg aactagtgtg tctgctacat ctactttaac tggtaatggt 1200
ggaactgaat ctggtggaac agctggaact actacgtcta gtggaactga agctggtgga 1260
actagtggaa ctactacgtc tagtggagct gctagtggta aagctggaac tggaacagct 1320
ggaactacta cgtctagtga aggtgctggt agtgataaag ctggaactgg aactagtgga 1380
actactacgt ctagtggaac tggtgctggt ggagctggta gtggtggacc tagtggacat 1440
gcttctaatg caaaaattcc tggaataatg acactaactc tatttgcatt attaacattt 1500
attgtaaatt gaatgaaaca catgatttat acattattat atattacaaa atttacacat 1560
tatttatgta tgaacgaacg aacatcttgc tcttaaataa agaaattgag atatatatgg 1620
aaatagatta aagtaacatg agaaagatga atataatatt agaatatgaa atttaacaga 1680
aataaaatga agtaaaagag tgtattttgt aataatttat aataaattag tatacaatga 1740
ttatattaca aatggctatt aaatatttta ttaattaaat attgattagt aatgatatta 1800
tgtatgtaca tgttagggtt gattgttata cattgtgaat atattatata attgtatatt 1860
atattgattg atataatgta gaggatattt ttttaaatag tatttaat 1908

<210> 51
<211> 1460
<212> DNA
<213> Babesia microti

<400> 51
aatccaacat ctagcctagt tagtatatat aggttaatat cacattatag attatctttg 60
gatgattggt tattatataa catgtcgctg aatgacgatt attttgctag ataatataac 120
taccggtgat tctgaggacc tactttaaag agaataatta acatatctac cagaatcagt 180
tccaatttat gtattttaaa gctaatcact actcgaaaac tacggtgaaa atggaaaaac 240
aagtggaagc tgtatgtcgt ggaaagtcac tacattttat gtgggcaaat ttaataattc 300
taaatactat gtttttgatg ttaaaaagcg aaaaacacac tttaatgcac attttaacat 360
catctgtata atatatatat cagcgttgaa atcatatggc aaaggtaata aagcgttaca 420
ttttgagcga ataaaggcac atatgcaaac gtatgaagcc ttgtatattt gtggaattat 480
attatgctag taatttgtga ttaataatgg caatatttat atacaaatat tcgagcgttc 540
tattatatgc atgcacataa ttaatcacaa actctcatat catggggcgg tttcgcccat 600
cataaacatt actgttagca ctctggtaga ttagcatggt gaatctctcg atacctgggc 660
tactgttgct ttccgcatat tccttaaatt ctgcaagtgc gggggatgta tatgagatat 720
cttctggtaa tccacccgac atagagccaa catctacttc tctagaaaca aatgtagtta 780
ccaactatat tccagaaccc aatgcggatt cagaatctgt acatgttgaa atccaggaac 840
atgataacat caatccacaa gacgcttgcg atagtgagcc gctcgaacaa atggattctg 900
ataccagggt gttgcccgaa agtttggatg aggggtacc acaccaattc tctagattag 960
ggcaccactc agacatggca tctgatataa atgatgaaga accatcattt aaaatcggcg 1020
agaatgacat aattcaacca ccctgggaag atacagctcc ataccattca atagatgatg 1080
aagagcttga caacttaatg agactaacgg cgcaagaaac aagtgacgat catgaagaag 1140
ggaatggcaa actcaatacg aataaaagtg agaagactga aagaaaatcg catgatactc 1200
agacaccgca agaaatatat gaagagcttg acaacttact gagactaacg gcacaagaaa 1260
tatatgaaga gcgtaaagaa gggcatggca aacccaatac gaataaaagt gagaaggctg 1320
aaagaaaatc gcatgatact cagacaacgc aagaaatatg tgaagagtgt gaagaagggc 1380
atgacaaaat caataagaat aaaagtggaa atgctggaat aaaatcgtat gatactcaga 1440
caccgcagga aacaagtgac 1460

<210> 52
<211> 503
<212> PRT
<213> Babesia microti

<400> 52
Lys Arg Phe Asn Glu His Thr Asp Met Asn Gly Ile His Tyr Tyr Tyr

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 1               5                  10                  15
Ile Asp Gly Ser Leu Leu Ala Ser Gly Glu Val Thr Ser Asn Phe Arg
            20                  25                  30
Tyr Ile Ser Lys Glu Tyr Glu Tyr Glu His Thr Glu Leu Ala Lys Glu
        35                  40                  45
His Cys Lys Lys Glu Lys Cys Val Asn Val Asp Asn Ile Glu Asp Asn
    50                  55                  60
Asn Leu Lys Ile Tyr Ala Lys Gln Phe Lys Ser Val Val Thr Thr Pro
65                  70                  75                  80
Ala Asp Val Ala Gly Val Ser Asp Gly Phe Phe Ile Arg Gly Gln Asn
                85                  90                  95
Leu Gly Ala Val Gly Ser Val Asn Glu Gln Pro Asn Thr Val Gly Met
            100                 105                 110
Ser Leu Glu Gln Phe Ile Lys Asn Glu Leu Tyr Ser Phe Ser Asn Glu
        115                 120                 125
Ile Tyr His Thr Ile Ser Ser Gln Ile Ser Asn Ser Phe Leu Ile Met
    130                 135                 140
Met Ser Asp Ala Ile Val Lys His Asp Asn Tyr Ile Leu Lys Lys Glu
145                 150                 155                 160
Gly Glu Gly Cys Glu Gln Ile Tyr Asn Tyr Glu Glu Phe Ile Glu Lys
                165                 170                 175
Leu Arg Gly Ala Arg Ser Glu Gly Asn Asn Met Phe Gln Glu Ala Leu
            180                 185                 190
Ile Arg Phe Arg Asn Ala Ser Ser Glu Glu Met Val Asn Ala Ala Ser
        195                 200                 205
Tyr Leu Ser Ala Ala Leu Phe Arg Tyr Lys Glu Phe Asp Asp Glu Leu
    210                 215                 220
Phe Lys Lys Ala Asn Asp Asn Phe Gly Arg Asp Asp Gly Tyr Asp Phe
225                 230                 235                 240
Asp Tyr Ile Asn Thr Lys Lys Glu Leu Val Ile Leu Ala Ser Val Leu
                245                 250                 255
Asp Gly Leu Asp Leu Ile Met Glu Arg Leu Ile Glu Asn Phe Ser Asp
            260                 265                 270
Val Asn Asn Thr Asp Asp Ile Lys Lys Ala Phe Asp Glu Cys Lys Ser
        275                 280                 285
Asn Ala Ile Ile Leu Lys Lys Lys Ile Leu Asp Asn Asp Glu Asp Tyr
    290                 295                 300
Lys Ile Asn Phe Arg Glu Met Val Asn Glu Val Thr Cys Ala Asn Thr
305                 310                 315                 320
Lys Phe Glu Ala Leu Asn Asp Leu Ile Ile Ser Asp Cys Glu Lys Lys
                325                 330                 335
Gly Ile Lys Ile Asn Arg Asp Val Ile Ser Ser Tyr Lys Leu Leu Leu
            340                 345                 350
Ser Thr Ile Thr Tyr Ile Val Gly Ala Gly Val Glu Ala Val Thr Val
        355                 360                 365
Ser Val Ser Ala Thr Ser Asn Gly Thr Glu Ser Gly Gly Ala Gly Ser
    370                 375                 380
Gly Thr Gly Thr Ser Val Ser Ala Thr Ser Thr Leu Thr Gly Asn Gly
385                 390                 395                 400
Gly Thr Glu Ser Gly Gly Thr Ala Gly Thr Thr Thr Ser Ser Gly Thr
                405                 410                 415
Glu Ala Gly Gly Thr Ser Gly Thr Thr Thr Ser Ser Gly Ala Ala Ser
            420                 425                 430
Gly Lys Ala Gly Thr Gly Thr Ala Gly Thr Thr Thr Ser Ser Glu Gly
        435                 440                 445
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Ala Gly Ser Asp Lys Ala Gly Thr Gly Thr Ser Gly Thr Thr Thr Ser
    450                 455                 460
Ser Gly Thr Gly Ala Gly Gly Ala Gly Ser Gly Gly Pro Ser Gly His
465                 470                 475                 480
Ala Ser Asn Ala Lys Ile Pro Gly Ile Met Thr Leu Thr Leu Phe Ala
                485                 490                 495
Leu Leu Thr Phe Ile Val Asn
            500
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<210> 53
<211> 275
<212> PRT
<213> Babesia microti

<400> 53

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Met Val Asn Leu Ser Ile Pro Gly Leu Leu Leu Leu Ser Ala Tyr Ser
 1               5                  10                  15
Leu Asn Ser Ala Ser Ala Gly Asp Val Tyr Glu Ile Ser Ser Gly Asn
            20                  25                  30
Pro Pro Asp Ile Glu Pro Thr Ser Thr Ser Leu Glu Thr Asn Val Val
        35                  40                  45
Thr Asn Tyr Ile Pro Glu Pro Asn Ala Asp Ser Glu Ser Val His Val
    50                  55                  60
Glu Ile Gln Glu His Asp Asn Ile Asn Pro Gln Asp Ala Cys Asp Ser
65                  70                  75                  80
Glu Pro Leu Glu Gln Met Asp Ser Asp Thr Arg Val Leu Pro Glu Ser
                85                  90                  95
Leu Asp Glu Gly Val Pro His Gln Phe Ser Arg Leu Gly His His Ser
            100                 105                 110
Asp Met Ala Ser Asp Ile Asn Asp Glu Glu Pro Ser Phe Lys Ile Gly
        115                 120                 125
Glu Asn Asp Ile Ile Gln Pro Arg Trp Glu Asp Thr Ala Pro Tyr His
    130                 135                 140
Ser Ile Asp Asp Glu Glu Leu Asp Asn Leu Met Arg Leu Thr Ala Gln
145                 150                 155                 160
Glu Thr Ser Asp Asp His Glu Glu Gly Asn Gly Lys Leu Asn Thr Asn
                165                 170                 175
Lys Ser Glu Lys Thr Glu Arg Lys Ser His Asp Thr Gln Thr Pro Gln
            180                 185                 190
Glu Ile Tyr Glu Glu Leu Asp Asn Leu Leu Arg Leu Thr Ala Gln Glu
        195                 200                 205
Ile Tyr Glu Glu Arg Lys Glu Gly His Gly Lys Pro Asn Thr Asn Lys
    210                 215                 220
Ser Glu Lys Ala Glu Arg Lys Ser His Asp Thr Gln Thr Thr Gln Glu
225                 230                 235                 240
Ile Cys Glu Glu Cys Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys
                245                 250                 255
Ser Gly Asn Ala Gly Ile Lys Ser Tyr Asp Thr Gln Thr Pro Gln Glu
            260                 265                 270
Thr Ser Asp
        275
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<210> 54
<211> 22
<212> DNA

<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 54
tttgcaggtg ataccgatcg cg 22

<210> 55
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 55
tggtattcta gaagaatagt tata 24

<210> 56
<211> 306
<212> DNA
<213> Babesia microti

<400> 56
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cccagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtggaactgt tgggcccagt gaagctggtg 120
ggcctagtga agctggtggg cctagtggaa ctggttggcc tagtgaagct ggtgggccta 180
gtggaactgt tgggcccagt gaagctggtg ggcctagtga agctggtggg cctagtggaa 240
ctggttggcc tagtggaact ggttggccta gtgaagttgg ttggcccatt gaaccatttg 300
gatatc 306

<210> 57
<211> 318
<212> DNA
<213> Babesia microti

<400> 57
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cccagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtggaactgt tgggcccagt gaagctggtg 120
ggcctagtga agctggtggg cctagtggaa ctggttggcc tagtgaagct ggtgggccta 180
gtggaactgt tgggcccagt gaagctggtg ggcctagtga agctggtggg cctagtggaa 240
ctggttggcc tagtggaact ggttggccta gtgaagttgg ttggcctaat gaaccatttg 300
gatatcacct tctttggt 318

<210> 58
<211> 358
<212> DNA
<213> Babesia microti

<400> 58
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt gaagctggtg ggcctagtga agctggttgg cctagtgaag 240

ctggttggcc tagtgaagct ggtgggccta gtggaactgg ttggcctagt gaagctggtt 300
ggcctagtga agctggttgg cctagtgaag ctggttggcc tagtgaagct ggttggcc 358

<210> 59
<211> 409
<212> DNA
<213> Babesia microti

<400> 59
tgcaggtgat accgatcgcg aagctggtgg gcctagtgga actgttgggc ctagtgaagc 60
tggtgggcct agtgaagctg gtgggcctag tgaagctggt gggcctagtg aagctggtgg 120
gcctagtgaa gctggtgggc ctagtgaagc tggtgggcct agtgaagctg gtgggcctag 180
tgaagctggt gggcctagtg aagctggtgg gcctagtgaa gctggttggc ctagtgaagc 240
tggttggcct agtgaagctg gtgggcctag tggaactggt tggcctagtg aagctggttg 300
gcctagtgaa gctggttggc ctagtgaagc tggttggcct agtgaagctg gttggcctag 360
tgaacgattt ggatatcagc ttctttggta ttctagaaga atagttata 409

<210> 60
<211> 351
<212> DNA
<213> Babesia microti

<400> 60
gtgaagctgg tgggcctagt ggaactgttg ggcctagtga agctggtggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt gaagctggtt ggcctagtga agctggttgg cctagtgaag 240
ctggtgggcc tagtggaact ggttggccta gtgaagctgg ttggcctagt gaagctggtt 300
ggcctagtga agctggttgg cctagtgaag ctggttggcc tagtgaacga t 351

<210> 61
<211> 410
<212> DNA
<213> Babesia microti

<400> 61
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tgggcctagt gaagctggtg ggcctagtga agctggtggg cctagtgaag ctggtgggcc 120
tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg ggcctagtga 180
agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg 240
ttggcctagt gaagctggtt ggcctagtga agctggtggg cctagtggaa ctggttggcc 300
tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt ggcctagtga 360
agctggttgg cctagtgaac gatttggata tcagcttctt tggtattcta 410

<210> 62
<211> 416
<212> DNA
<213> Babesia microti

<400> 62
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt gaagctggtg ggcctagtga agctggtggg cctagtgaag 240
ctggtgggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtg 300

ggcctagtgg aactggttgg cctagtgaag ctggttggcc tagtgaagct ggttggccta 360
gtgaagctgg ttggcctagt gaagctggtt ggcctagtga acgatttgga tatcag 416

<210> 63
<211> 356
<212> DNA
<213> Babesia microti

<400> 63
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt ggaactggtt ggcctagtga agctggttgg cctagtgaag 240
ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt 300
ggcctagtga acgatttgga tatcagcttc tttggtattc tagaagaata gttata 356

<210> 64
<211> 285
<212> DNA
<213> Babesia microti

<400> 64
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtggaactgg ttggcctagt gaagctggtt ggcctagtga agctggttgg cctagtgaag 240
ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggc 285

<210> 65
<211> 342
<212> DNA
<213> Babesia microti

<400> 65
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt ggaactggtt ggcctagtga agctggttgg cctagtgaag 240
ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt 300
ggcctagtga acgatttgga tatcagcttc tttggtattc ta 342

<210> 66
<211> 363
<212> DNA
<213> Babesia microti

<400> 66
ttgcaggtga taccgatcgc gaagctggtg ggcctagtgg aactgttggg cctagtgaag 60
ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
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ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt 300
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gaa 363

<210> 67
<211> 363
<212> DNA
<213> Babesia microti

<400> 67
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ctggtgggcc tagtgaagct ggtgggccta gtgaagctgg tgggcctagt gaagctggtg 120
ggcctagtga agctggtggg cctagtgaag ctggtgggcc tagtgaagct ggtgggccta 180
gtgaagctgg tgggcctagt gaagctggtg ggcctagtgg aactggttgg cctagtgaag 240
ctggttggcc tagtgaagct ggttggccta gtgaagctgg ttggcctagt gaagctggtt 300
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gaa 363

<210> 68
<211> 101
<212> PRT
<213> Babesia microti

<400> 68
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1 5 10 15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
20 25 30
Val Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Gly Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
65 70 75 80
Gly Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Val Gly Trp Pro Ile
85 90 95
Glu Pro Phe Gly Tyr
100

<210> 69
<211> 105
<212> PRT
<213> Babesia microti

<400> 69
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
1 5 10 15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
20 25 30
Val Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Gly Thr Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr
65 70 75 80
Gly Trp Pro Ser Gly Thr Gly Trp Pro Ser Glu Val Gly Trp Pro Asn
85 90 95
Glu Pro Phe Gly Tyr His Leu Leu Trp
100 105

<210> 70
<211> 118
<212> PRT
<213> Babesia microti

<400> 70
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Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
20 25 30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65 70 75 80
Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser
85 90 95
Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp
100 105 110
Pro Ser Glu Ala Gly Trp
115

<210> 71
<211> 136
<212> PRT
<213> Babesia microti

<400> 71
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
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Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
20 25 30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65 70 75 80
Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser
85 90 95
Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp
100 105 110
Pro Ser Glu Ala Gly Trp Pro Ser Glu Arg Phe Gly Tyr Gln Leu Leu
115 120 125
Trp Tyr Ser Arg Arg Ile Val Ile
130 135

<210> 72
<211> 116
<212> PRT
<213> Babesia microti

<400> 72

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Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
            20                  25                  30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
        35                  40                  45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
    50                  55                  60
Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65                  70                  75                  80
Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
                85                  90                  95
Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp
            100                 105                 110
Pro Ser Glu Arg
        115

      <210> 73
      <211> 136
      <212> PRT
      <213> Babesia microti

      <400> 73
Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly Pro
 1               5                  10                  15
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            20                  25                  30
Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu
        35                  40                  45
Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro
    50                  55                  60
Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly
65                  70                  75                  80
Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Gly Pro Ser Gly
                85                  90                  95
Thr Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro
            100                 105                 110
Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Arg Phe
        115                 120                 125
Gly Tyr Gln Leu Leu Trp Tyr Ser
    130                 135

      <210> 74
      <211> 138
      <212> PRT
      <213> Babesia microti

      <400> 74
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
 1               5                  10                  15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
            20                  25                  30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
        35                  40                  45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
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    50                  55                  60
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
65                  70                  75                  80
Gly Gly Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
                85                  90                  95
Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp
            100                 105                 110
Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
        115                 120                 125
Gly Trp Pro Ser Glu Arg Phe Gly Tyr Gln
    130                 135

      <210> 75
      <211> 118
      <212> PRT
      <213> Babesia microti

      <400> 75
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
 1               5                  10                  15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
            20                  25                  30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
        35                  40                  45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
    50                  55                  60
Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65                  70                  75                  80
Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
                85                  90                  95
Glu Ala Gly Trp Pro Ser Glu Arg Phe Gly Tyr Gln Leu Leu Trp Tyr
            100                 105                 110
Ser Arg Arg Ile Val Ile
        115

      <210> 76
      <211> 94
      <212> PRT
      <213> Babesia microti

      <400> 76
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
 1               5                  10                  15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
            20                  25                  30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
        35                  40                  45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp
    50                  55                  60
Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65                  70                  75                  80
Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp
                85                  90

      <210> 77
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<211> 113
<212> PRT
<213> Babesia microti

<400> 77
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
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Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
20 25 30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
50 55 60
Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala
65 70 75 80
Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
85 90 95
Glu Ala Gly Trp Pro Ser Glu Arg Phe Gly Tyr Gln Leu Leu Trp Tyr
100 105 110
Ser

<210> 78
<211> 120
<212> PRT
<213> Babesia microti

<400> 78
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
1 5 10 15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
20 25 30
Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala
65 70 75 80
Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
85 90 95
Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Arg Phe Gly
100 105 110
Tyr Gln Leu Leu Trp Tyr Ser Arg
115 120

<210> 79
<211> 120
<212> PRT
<213> Babesia microti

<400> 79
Ala Gly Asp Thr Asp Arg Glu Ala Gly Gly Pro Ser Gly Thr Val Gly
1 5 10 15
Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala
20 25 30

Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser
35 40 45
Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly Pro Ser Glu Ala Gly Gly
50 55 60
Pro Ser Glu Ala Gly Gly Pro Ser Gly Thr Gly Trp Pro Ser Glu Ala
65 70 75 80
Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser
85 90 95
Glu Ala Gly Trp Pro Ser Glu Ala Gly Trp Pro Ser Glu Arg Phe Gly
100 105 110
Tyr Gln Leu Leu Trp Tyr Ser Arg
115 120

<210> 80
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 80
cagagcagta ctgatgatat taagaaggc 29

<210> 81
<211> 43
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 81
caatatgaat tcagtgaata tttacaataa atgttaataa tgc 43

<210> 82
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 82
cataacaata ttccagaacc caatgcggat tc 32

<210> 83
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR Primer

<400> 83

cgctagaatt cattagaaag ccttaaacat gc 32

<210> 84
<211> 2001
<212> DNA
<213> Babesia

<400> 84
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tttagggaaa tggtgaatga agtaacatgt gcaaacacaa aatttgaagc cctaaatgat 180
ttgataattt ccgactgtga gaaaaaaggt attaagataa acagagatgt gatttcaagc 240
tacaaattgc ttctttccac aatcacctat attgttggag ctggagttga agctgtaact 300
gttagtgtgt ctgctacatc taatggaact gaatctggtg gagctggtag tggaactgga 360
actagtgtgt ctgctacatc tactttaact ggtaatggtg gaactgaatc tggtggaaca 420
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<210> 85
<211> 667
<212> PRT
<213> Babesia

<400> 85
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20 25 30

Asn Asp Glu Asp Tyr Lys Ile Asn Phe Arg Glu Met Val Asn Glu Val
35 40 45

Thr Cys Ala Asn Thr Lys Phe Glu Ala Leu Asn Asp Leu Ile Ile Ser
50 55 60

Asp Cys Glu Lys Lys Gly Ile Lys Ile Asn Arg Asp Val Ile Ser Ser
65 70 75 80

Tyr Lys Leu Leu Leu Ser Thr Ile Thr Tyr Ile Val Gly Ala Gly Val
85 90 95

Glu Ala Val Thr Val Ser Val Ser Ala Thr Ser Asn Gly Thr Glu Ser
100 105 110

Gly Gly Ala Gly Ser Gly Thr Gly Thr Ser Val Ser Ala Thr Ser Thr
115 120 125

Leu Thr Gly Asn Gly Gly Thr Glu Ser Gly Gly Thr Ala Gly Thr Thr
130 135 140

Thr Ser Ser Gly Thr Glu Ala Gly Gly Thr Ser Gly Thr Thr Thr Ser
145 150 155 160

Ser Gly Ala Ala Ser Gly Lys Ala Gly Thr Gly Thr Ala Gly Thr Thr
165 170 175

Thr Ser Ser Glu Gly Ala Gly Ser Asp Lys Ala Gly Thr Gly Thr Ser
180 185 190

Gly Thr Thr Thr Ser Ser Gly Thr Gly Ala Gly Gly Ala Gly Ser Gly
195 200 205

Gly Pro Ser Gly His Ala Ser Asn Ala Lys Ile Pro Gly Ile Met Thr
210 215 220

Leu Thr Leu Phe Ala Leu Leu Thr Phe Ile Val Asn Ile Pro Glu Pro
225 230 235 240

Asn Ala Asp Ser Glu Ser Val His Val Glu Ile Gln Glu His Asp Asn
245 250 255

Ile Asn Pro Gln Asp Ala Cys Asp Ser Glu Pro Leu Glu Gln Met Asp
260 265 270

Ser Asp Thr Arg Val Leu Pro Glu Ser Leu Asp Glu Gly Val Pro His
275 280 285

Gln Phe Ser Arg Leu Gly His His Ser Asp Met Ala Ser Asp Ile Asn
290 295 300

Asp Glu Glu Pro Ser Phe Lys Ile Gly Glu Asn Asp Ile Ile Gln Pro
305 310 315 320

Pro Trp Glu Asp Thr Ala Pro Tyr His Ser Ile Asp Asp Glu Glu Leu

325 330 335

Asp Asn Leu Met Arg Leu Thr Ala Gln Glu Thr Ser Asp Asp His Glu
340 345 350

Glu Gly Asn Gly Lys Leu Asn Thr Asn Lys Ser Glu Lys Thr Glu Arg
355 360 365

Lys Ser His Asp Thr Gln Thr Pro Gln Glu Ile Tyr Glu Glu Leu Asp
370 375 380

Asn Leu Leu Arg Leu Thr Ala Gln Glu Ile Tyr Glu Glu Arg Lys Glu
385 390 395 400

Gly His Gly Lys Pro Asn Thr Asn Lys Ser Glu Lys Ala Glu Arg Lys
405 410 415

Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu Cys Glu Glu
420 425 430

Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly Ile Lys
435 440 445

Ser Tyr Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu Cys Glu Glu
450 455 460

Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly Ile Lys
465 470 475 480

Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala His Glu Glu
485 490 495

Gly His Asp Lys Ile Asn Thr Asn Lys Ser Glu Lys Ala Glu Arg Lys
500 505 510

Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu Cys Glu Glu
515 520 525

Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly Ile Lys
530 535 540

Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala His Glu Glu
545 550 555 560

Glu His Gly Asn Leu Asn Lys Asn Lys Ser Gly Lys Ala Gly Ile Lys
565 570 575

Ser His Asn Thr Gln Thr Pro Leu Lys Lys Lys Asp Phe Cys Lys Glu
580 585 590

Gly Cys His Gly Cys Asn Asn Lys Pro Glu Asp Asn Glu Arg Asp Pro
595 600 605

Ser Ser Pro Asp Asp Asp Gly Gly Cys Glu Cys Gly Met Thr Asn His
610 615 620

Phe Val Phe Asp Tyr Lys Thr Thr Leu Leu Leu Lys Ser Leu Lys Thr
625 630 635 640

Glu Thr Ser Thr His Tyr Tyr Ile Ala Met Ala Ala Ile Phe Thr Ile
645 650 655

Ser Leu Phe Pro Cys Met Phe Lys Ala Phe
660 665

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<211> 3402
<212> DNA
<213> Babesia

<400> 86
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gaagattttg acggaataca aacactttta caagtgtcta tcattgctag ttacggtcca 180
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gaattactgt tggaagtact cgagaacccc tctttcccta gtgcaattag caattacacc 660
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<210> 87
<211> 1134
<212> PRT
<213> Babesia

<400> 87

Met Gln His His His His His His Leu Thr Phe Gly Asn Ile Arg Phe
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His Asn Ile Asn Leu Pro Pro Phe Ser Leu Gly Ile Ile His Ser Ile
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Thr Val Glu Lys Ala Ile Asn Ser Glu Asp Phe Asp Gly Ile Gln Thr
35 40 45

Leu Leu Gln Val Ser Ile Ile Ala Ser Tyr Gly Pro Ser Gly Asp Tyr
50 55 60

Ser Ser Phe Val Phe Thr Pro Val Val Thr Ala Asp Thr Asn Val Phe
65 70 75 80

Tyr Lys Leu Glu Thr Asp Phe Lys Leu Asp Val Asp Val Ile Thr Lys
85 90 95

Thr Ser Leu Glu Leu Pro Thr Ser Val Pro Gly Phe His Tyr Thr Glu
100 105 110

Thr Ile Tyr Gln Gly Thr Glu Leu Ser Lys Phe Ser Lys Pro Gln Cys
115 120 125

Lys Leu Asn Asp Pro Pro Ile Thr Thr Gly Ser Gly Leu Gln Ile Ile
130 135 140

His Asp Gly Leu Asn Asn Ser Thr Ile Ile Thr Asn Lys Glu Val Asn
145 150 155 160

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Val Asp Gly Thr Asp Leu Val Phe Phe Glu Leu Leu Pro Pro Ser Asp
                165                 170                 175

Gly Ile Pro Thr Leu Arg Ser Lys Leu Phe Pro Val Leu Lys Ser Ile
            180                 185                 190

Pro Met Ile Ser Thr Gly Val Asn Glu Leu Leu Leu Glu Val Leu Glu
        195                 200                 205

Asn Pro Ser Phe Pro Ser Ala Ile Ser Asn Tyr Thr Gly Leu Thr Gly
    210                 215                 220

Arg Leu Asn Lys Leu Leu Thr Val Leu Asp Gly Ile Val Asp Ser Ala
225                 230                 235                 240

Ile Ser Val Lys Thr Thr Glu Thr Val Pro Asp Asp Ala Glu Thr Ser
                245                 250                 255

Ile Ser Ser Leu Lys Ser Leu Ile Lys Ala Ile Arg Asp Asn Ile Thr
            260                 265                 270

Thr Thr Arg Asn Glu Val Thr Lys Asp Asp Val Tyr Ala Leu Lys Lys
        275                 280                 285

Ala Leu Thr Cys Leu Thr Thr His Leu Ile Tyr His Ser Lys Val Asp
    290                 295                 300

Gly Ile Ser Phe Asp Met Leu Gly Thr Gln Lys Asn Lys Ser Ser Pro
305                 310                 315                 320

Leu Gly Lys Ile Gly Thr Ser Met Asp Asp Ile Ile Ala Met Phe Ser
                325                 330                 335

Asn Pro Asn Met Tyr Leu Val Lys Val Ala Tyr Leu Gln Ala Ile Glu
            340                 345                 350

His Ile Phe Leu Ile Ser Thr Lys Tyr Asn Asp Ile Phe Asp Tyr Thr
        355                 360                 365

Ile Asp Phe Ser Lys Arg Glu Ala Thr Asp Ser Gly Ser Phe Thr Asp
    370                 375                 380

Ile Leu Leu Gly Asn Lys Val Lys Glu Ser Leu Ser Phe Ile Glu Gly
385                 390                 395                 400

Leu Ile Ser Asp Ile Lys Ser His Ser Leu Lys Ala Gly Val Thr Gly
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Gly Ile Ser Ser Ser Ser Leu Phe Asp Glu Ile Phe Asp Glu Leu Asn
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Leu Asp Gln Ala Thr Ile Arg Thr Leu Val Ala Pro Leu Asp Trp Pro
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Leu Ile Ser Asp Lys Ser Leu His Pro Ser Leu Lys Met Val Val Val
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Ala Phe Asp Glu Cys Lys Ser Asn Ala Ile Ile Leu Lys Lys Lys Ile
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Leu Asp Asn Asp Glu Asp Tyr Lys Ile Asn Phe Arg Glu Met Val Asn
            500                 505                 510

Glu Val Thr Cys Ala Asn Thr Lys Phe Glu Ala Leu Asn Asp Leu Ile
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Ile Ser Asp Cys Glu Lys Lys Gly Ile Lys Ile Asn Arg Asp Val Ile
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Ser Ser Tyr Lys Leu Leu Leu Ser Thr Ile Thr Tyr Ile Val Gly Ala
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Gly Val Glu Ala Val Thr Val Ser Val Ser Ala Thr Ser Asn Gly Thr
                565                 570                 575

Glu Ser Gly Gly Ala Gly Ser Gly Thr Gly Thr Ser Val Ser Ala Thr
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Ser Thr Leu Thr Gly Asn Gly Gly Thr Glu Ser Gly Gly Thr Ala Gly
        595                 600                 605

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Thr Thr Thr Ser Ser Glu Gly Ala Gly Ser Asp Lys Ala Gly Thr Gly
                645                 650                 655

Thr Ser Gly Thr Thr Thr Ser Ser Gly Thr Gly Ala Gly Gly Ala Gly
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Ser Gly Gly Pro Ser Gly His Ala Ser Asn Ala Lys Ile Pro Gly Ile
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Pro His Gln Phe Ser Arg Leu Gly His His Ser Asp Met Ala Ser Asp
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Gln Pro Pro Trp Glu Asp Thr Ala Pro Tyr His Ser Ile Asp Asp Glu
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Glu Leu Asp Asn Leu Met Arg Leu Thr Ala Gln Glu Thr Ser Asp Asp
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His Glu Glu Gly Asn Gly Lys Leu Asn Thr Asn Lys Ser Glu Lys Thr
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Glu Arg Lys Ser His Asp Thr Gln Thr Pro Gln Glu Ile Tyr Glu Glu
        835                 840                 845

Leu Asp Asn Leu Leu Arg Leu Thr Ala Gln Glu Ile Tyr Glu Glu Arg
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Lys Glu Gly His Gly Lys Pro Asn Thr Asn Lys Ser Glu Lys Ala Glu
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Arg Lys Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu Cys
                885                 890                 895

Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly
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Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly
    930                 935                 940

Ile Lys Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala His
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Glu Glu Gly His Asp Lys Ile Asn Thr Asn Lys Ser Glu Lys Ala Glu
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Arg Lys Ser His Asp Thr Gln Thr Thr Gln Glu Ile Cys Glu Glu Cys
            980                 985                 990

Glu Glu Gly His Asp Lys Ile Asn Lys Asn Lys Ser Gly Asn Ala Gly
        995                 1000                1005

Ile Lys Ser Tyr Asp Thr Gln Thr Pro Gln Glu Thr Ser Asp Ala His
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Glu Glu Glu His Gly Asn Leu Asn Lys Asn Lys Ser Gly Lys Ala Gly
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Ile Lys Ser His Asn Thr Gln Thr Pro Leu Lys Lys Lys Asp Phe Cys
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Lys Glu Gly Cys His Gly Cys Asn Asn Lys Pro Glu Asp Asn Glu Arg
1060 1065 1070

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Asn His Phe Val Phe Asp Tyr Lys Thr Thr Leu Leu Leu Lys Ser Leu
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<223> PCR Primer

<400> 90
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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 00/09136

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/30 C07K14/44 C12N15/62 G01N33/569 C12Q1/68
C07K16/20 A61K39/018

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, PAJ, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,L	EP 0 834 567 A (CORIXA CORP) 8 April 1998 (1998-04-08) the whole document L: priority	1-67
P,X,L	WO 99 29869 A (CORIXA CORP ;MAYO FOUNDATION (US)) 17 June 1999 (1999-06-17) the whole document L: priority	1-67

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 July 2000	24/07/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lejeune, R

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/US 00/09136

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0834567 A	08-04-1998	NONE	
WO 9929869 A	17-06-1999	AU 1820499 A	28-06-1999

PATENT COOPERATION TREATY

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SEED INTELLECTUAL PROPERTY LAW GROUP PLLC

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From the INTERNATIONAL SEARCHING AUTHORITY

To:
SEED INTELLECTUAL PROPERTY LAW
GROUP PLLC
Attn. Potter, Jane E.R.
Suite 6300
701 Fifth Avenue
Seattle, WA 98104-7092
UNITED STATES OF AMERICA

RECOMMANDEE

SUPP. IDS. AUG. 4, 2002

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference 210121.42603	Date of mailing (day/month/year) 05/07/2002
International application No. PCT/US 01/15192	PAYMENT DUE within 45 ~~months~~/days from the above date of mailing
Applicant CORIXA CORPORATION et al.	International filing date (day/month/year) 09/05/2001

PCT-ADD. FEES AUG. 19, 2002

1. This International Searching Authority

(i) considers that there are 28 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

(ii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:
in part 1-34, 36 (all as far as possible

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00 (Fee per additional invention) x 27 (number of additional inventions) = EUR 25.515,00 (total amount of additional fees)

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. further info have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Henriëtte Huysing-Solles

Form PCT/ISA/206 (July 1992)

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US 01/15192

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
√X,L	EP 0 834 567 A (CORIXA CORP) 8 April 1998 (1998-04-08) (L: Priority) the whole document ---	1-34,36
P,X,L	WO 00 60090 A (CORIXA CORP ;REED STEVEN G (US); SLEATH PAUL R (US); LODES MICHAEL) 12 October 2000 (2000-10-12) (L: Priority) the whole document ---	1-34,36
√X,L	WO 99 29869 A (CORIXA CORP ;MAYO FOUNDATION (US)) 17 June 1999 (1999-06-17) (L: Priority) the whole document -----	1-34,36

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"&" document member of the same patent family

Patent Family Ann x

Information on patent family members

International Application No
PCT/US 01/15192

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0834567 A	08-04-1998	US 6306396 B1	23-10-2001
		US 6183976 B1	06-02-2001
		EP 0834567 A2	08-04-1998
		US 2001029295 A1	11-10-2001
		US 6214971 B1	10-04-2001
WO 0060090 A	12-10-2000	AU 4204700 A	23-10-2000
		EP 1169455 A1	09-01-2002
		WO 0060090 A1	12-10-2000
		US 2001029295 A1	11-10-2001
WO 9929869 A	17-06-1999	US 6214971 B1	10-04-2001
		AU 1820499 A	28-06-1999
		WO 9929869 A1	17-06-1999
		US 2001029295 A1	11-10-2001